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BLOOD PLASMA IN MULTIPLE SCLEROSIS

Periodic Abnormalities in Pattern of Paper Chromatograms

ROY L. SWANK, M.D.
MONTREAL, CANADA

IN A PREVIOUS investigation Swank, Franklin, and Quastel [1] found that the plasma protein pattern in paper chromatograms may be abnormal during exacerbations of multiple sclerosis. During remission the plasma protein pattern returns to normal. Using the ultracentrifuge, Aird, Gofman, Jones, Campbell, and Garoutte [2] observed the presence of abnormal plasma lipoprotein fractions during activity of the disease. The fact that these abnormal lipoproteins occurred during exacerbations suggests that they are in some way related to the previous observation of Swank, Franklin, and Quastel.[1] However, no decision is yet justified.

The purpose of the present paper is to demonstrate the normal paper chromatogram and its changes when studied frequently over long periods of time in normal human subjects, and in patients with multiple sclerosis during periods both of activity and of relative inactivity of the disease.

MATERIAL AND METHODS

Blood samples were obtained from fasting patients and fasting normal subjects at weekly or shorter intervals and prevented from clotting with heparin. Many of the patients were on low-fat diets [3] for much of the study period. They were all ambulant, and most of them were capable of working full time. The capillary ascent method of chromatographic analysis,[4] as used by Franklin and Quastel,[5] was employed. The same method was used before by Swank, Franklin, and Quastel [1] in their study of multiple sclerosis during exacerbation of the disease. In the present study four sets of conditions were used for each chromatogram: 0.02 and 0.04 ml. of poly-

Miss Aagot Grimsgaard gave technical assistance.

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

Supported by a National Health Grant from the Department of National Health and Welfare, Ottawa, Ont., and the Multiple Sclerosis Society of Canada.

1. Swank, R. L.; Franklin, A. E., and Quastel, J. H.: Paper Chromatography of Blood Plasmas in Multiple Sclerosis, Proc. Soc. Exper. Biol. & Med. **76**:183-189, 1951.

2. Aird, R. B.; Gofman, J.; Jones, H. B.; Campbell, B., and Garoutte, B: Ultracentrifuge Studies on Lipoproteins in the Cerebrospinal Fluid and Serum of Patients with Multiple Sclerosis, read before the Fourth Annual Meeting of the American Academy of Neurology, Louisville, Ky., April 25, 1952.

3. Swank, R. L.: Treatment of Multiple Sclerosis with Low-Fat Diet, A. M. A. Arch. Neurol. & Psychiat. **69**:91-103, 1953.

4. Williams, R. J., and Kirby, H.: Paper Chromatography Using Capillary Ascent, Science **107**:481-483, 1948.

5. Franklin, A. E., and Quastel, J. H.: Paper Chromatography of Protein Mixture and Blood Plasmas, Proc. Soc. Exper. Biol. & Med. **74**:803-808, 1950.

oxyethylene sorbitan monooleate (tween® 81) and 0.01 and 0.03 ml. of polyoxyethylene sorbitan trioleate (tween® 85) per 0.5 ml. of the test plasma. The method of preparation of the plasma was the same as that employed before.[1] In the present study the papers were attached to a right-angled frame and held flat during ascent of the solvent. Sixteen to 20 frames were attached to a rack and immersed in solvent simultaneously. After ascent of the solvent the rack could be elevated in the chromatographic box and the tray of fluid removed. Heat was then applied to the bottom of the chromatographic box to speed the drying of the papers. When the papers had dried, the entire rack was rotated 90 degrees and the papers reimmersed in the second solvent for ascent in the second dimension. Drying was accomplished as before. Two sets of papers were processed daily, making it possible for one technician to do 8 to 10 chromatograms daily, each with four conditions. Plasmas from normal subjects and from patients were processed together on the same days. One series of studies was carried out between January and June, 1951, and a second series, between December, 1951, and June, 1952.

The sedimentation rate was determined on each blood sample, using Wintrobe tubes and noting the sedimentation reading at the end of one hour.

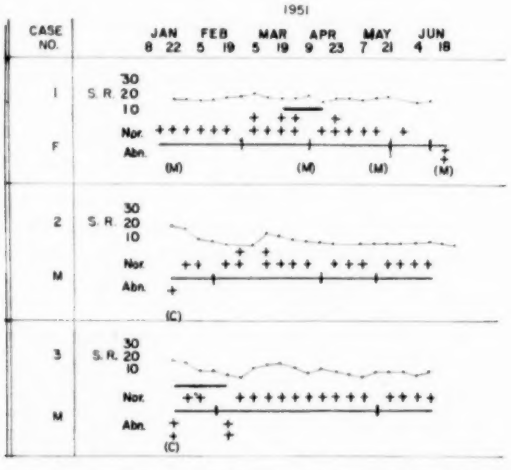

Fig. 1.—Distribution of normal (*Nor.*), abnormal (*Abn.*), and questionably normal (a single line across the base line) chromatograms taken at weekly intervals in normal subjects. The sedimentation rate (*S.R.*) is also recorded. The short dark, heavy line, between the record of the sedimentation rate and the chromatogram record in Cases 1 and 3 refers to the chromatograms illustrated in Figures 2 and 3, for menstruation (*M*) and cold (*C*) respectively.

RESULTS

The Paper Chromatogram for Normal Subjects.—Two hundred forty-three chromatograms from 21 normal human subjects were studied. Six of these subjects were studied at weekly intervals for approximately five months; two, for four months; five, for two to three months, and eight, for three weeks to two months.

The chromatograms, repeated at weekly intervals, revealed a surprising regularity of the plasma protein patterns in all but three of the normal subjects, two of whom were sisters of patients with multiple sclerosis. In the remaining 18 normal subjects there occurred periodically questionably normal (±) patterns or an occasional pattern which was considered abnormal because it was similar to the abnormal patterns seen frequently in patients with multiple sclerosis. These recurred at

intervals of one to three months, as shown in Figure 1 (Cases 1 to 3). Two representative series of chromatograms from normal subjects are shown in Figures 2 and 3. These figures illustrate the maximum variability in the pattern of plasma proteins to be seen in normal subjects. When records taken during complicating "colds," records from two siblings of patients with multiple sclerosis, and records from an apparently normal subject with only one normal chromatogram in a series

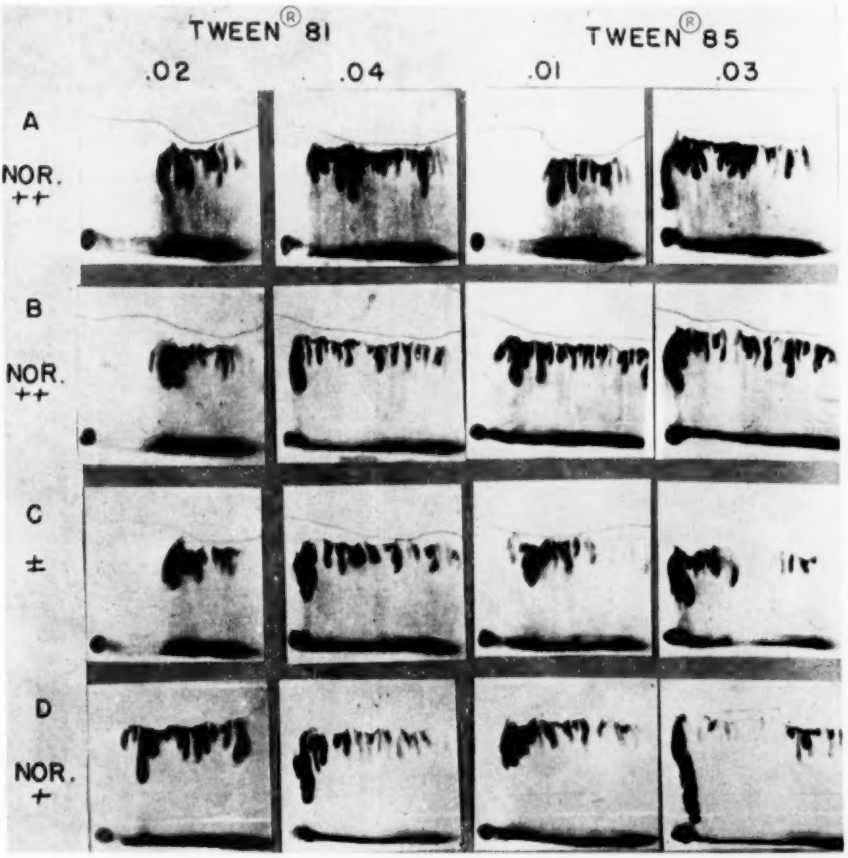

Fig. 2.—Series of four chromatograms (*A*, *B*, *C*, and *D*) taken at weekly intervals from a normal female subject (Case 1; Fig. 1). Each chromatogram consists of four conditions, 0.02 and 0.04 polyoxyethylene sorbitan monooleate (tween® 81) and 0.01 and 0.03 polyoxyethylene sorbitan trioleate (tween® 85). *Nor.* indicates normal; *Abn.*, abnormal, and ±, questionably normal.

of seven were eliminated from those normal for the subjects, approximately 4% of the records were similar to the abnormal chromatograms seen frequently for patients with multiple sclerosis. An additional approximately 15% of the records were considered questionably normal (±). About half of these questionably normal

records were obtained from females during menstruation. The remaining 81% of the records were considered normal.

The + type of normal chromatograms (Figs. 2 *D* and 3 *B* and *C*) usually has more than 15, and frequently more than 20, component fractions in at least three

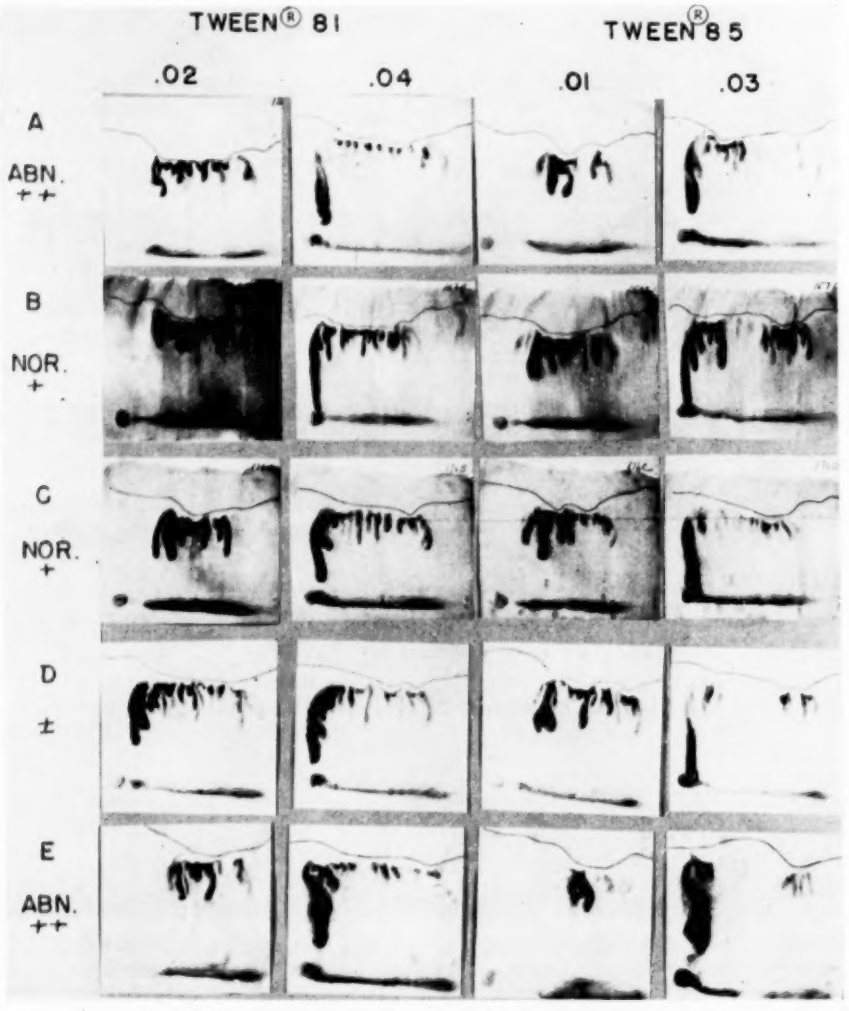

Fig. 3.—Series of five chromatograms taken at weekly intervals from a normal male subject (Case 3; Fig. 1). The maximum change observed in this subject is illustrated.

conditions. In these conditions the vertical dimension of most of the individual fractions is usually greater than the horizontal dimension by several or more times. In the ++ type of normal chromatograms (Fig. 2 *A* and *B*) the individual fractions are better developed and more distinct than in the + types of normal records.

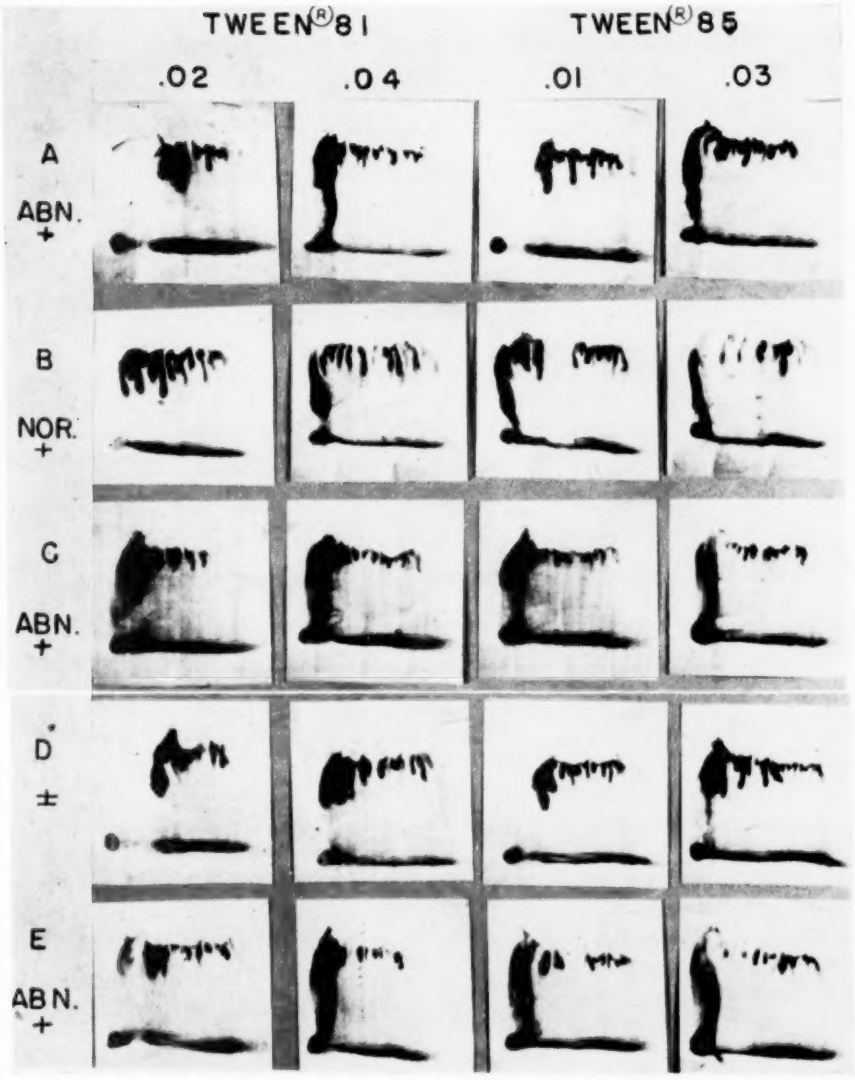

Fig. 4.—Series of two chromatograms (*D* and *E*) from a female patient with multiple sclerosis, and another series, of three chromatograms (*A*, *B*, and *C*), from her normal identical twin sister. Note the similarity of *A* and *C* to *D* and *E*.

The questionably normal records (Figs. 2*C* and 3*D*) are characterized by less well-developed fractions, by fewer fractions, by a tendency for the individual fractions to be shortened, and/or by a tendency for much of the protein to be retained

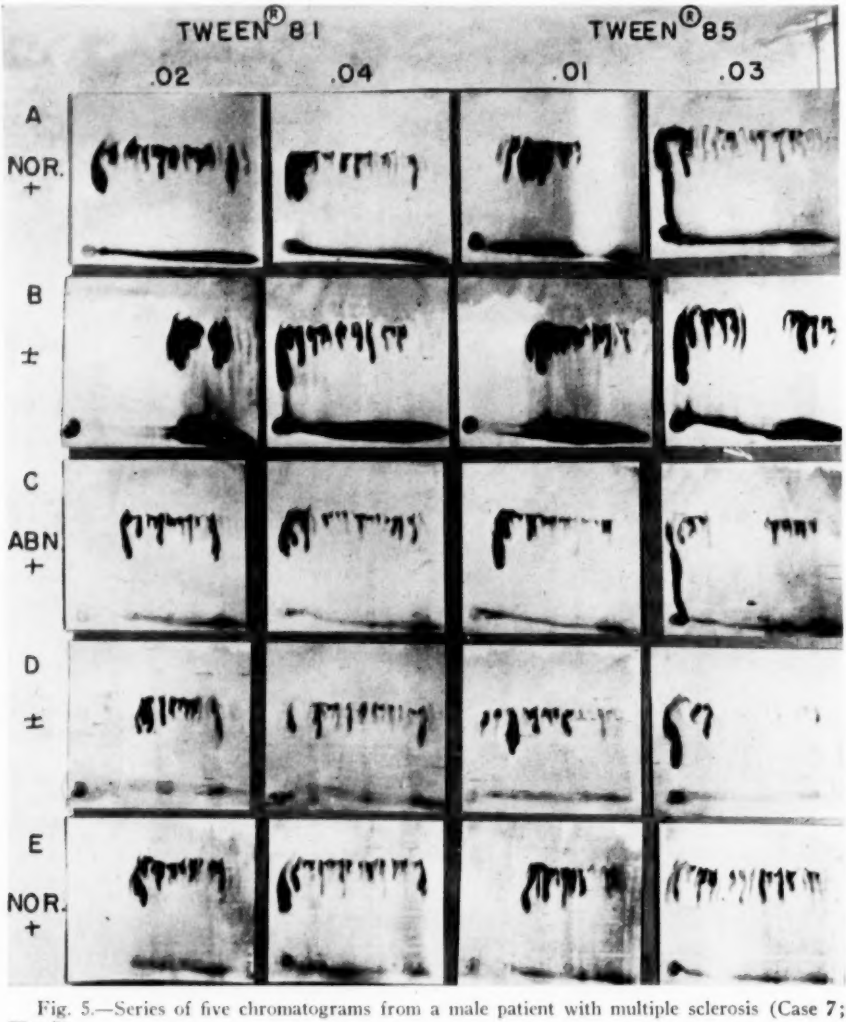

Fig. 5.—Series of five chromatograms from a male patient with multiple sclerosis (Case 7; Fig. 7).

at, or be connected with, the point of origin of the plasma in at least three conditions. The three types of abnormal records seen infrequently for normal subjects and frequently for patients with multiple sclerosis will be described in the next section. It is important to note that the pattern of plasma proteins of most normal subjects

became questionably normal at one- to three-month intervals (Fig. 1). This shift appeared to be in the same direction as was observed in the patients, only it was much less marked.

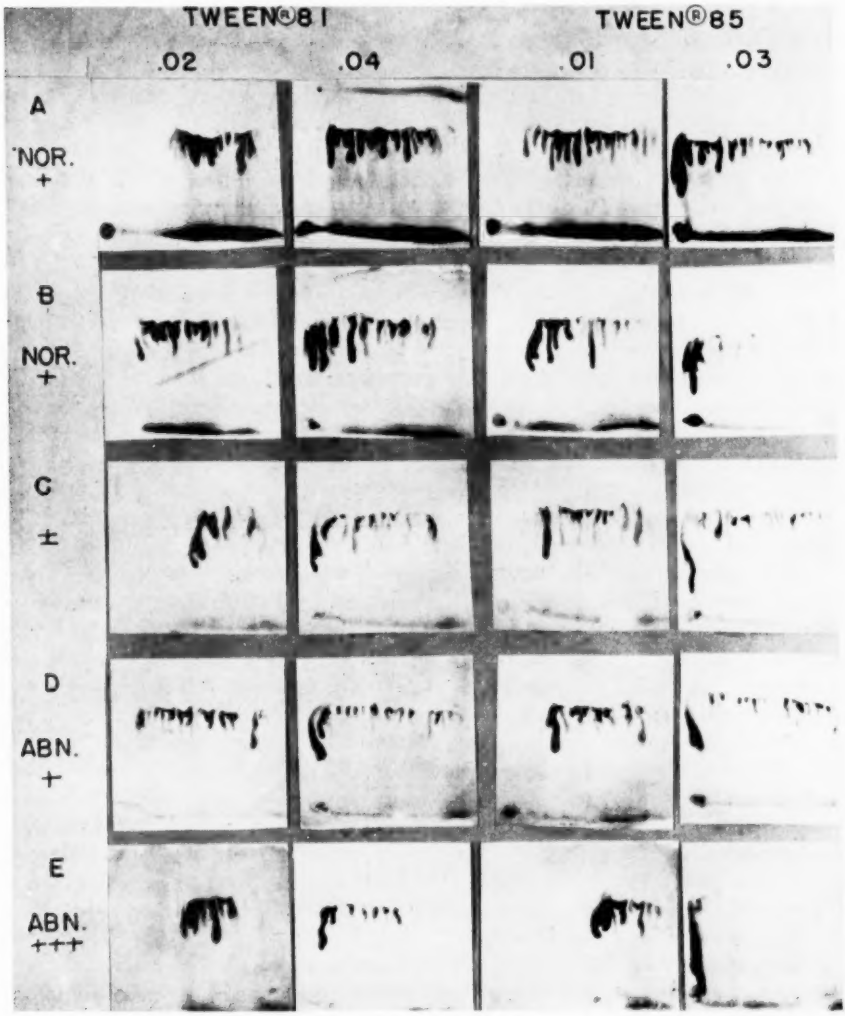

Fig. 6.—Series of five chromatograms from a female patient with multiple sclerosis (Case 6; Fig. 7).

A definite change occurred in the plasma protein pattern during the menstrual cycle (Fig. 2*C*). The chromatogram became first questionably normal and then occasionally abnormal (+ or ++). These changes did not always take place at the same time in relation to the menses. The maximum change in the chromatograms was observed sometimes a few days before and sometimes during menstruation,

but usually it seemed to coincide most nearly with the day of onset of menstruation. This statement is based on the study of 41 chromatograms taken at two- to three-day intervals before, during, and after 11 menstrual periods. Definite so-called abnormal records (+, ++, and +++) were observed also during the common cold in some subjects (Fig. 3 *A*). In one woman all of a series of four chromatograms studied at weekly intervals during an extended cold were abnormal.

From two clinically normal blood relatives of patients (one an identical twin sister and the other a sister) frequent abnormal records were obtained. Sample chromatograms from the patient with multiple sclerosis (Fig. 4 *D* and *E*) and her identical twin sister (Fig. 4 *A*, *B*, and *C*) show strikingly similar abnormalities.

One apparently normal male subject had four abnormal, two questionably normal, and one normal record in a series of seven chromatograms taken at weekly intervals. There was no explanation for the overwhelming predominance of abnormal records in this "normal" human subject.

The Paper Chromatogram for Patients with Multiple Sclerosis.—Four hundred thirty-seven chromatograms were studied from 41 patients with multiple sclerosis. Ten patients were studied at weekly intervals over a period of five months; 4 were studied similarly for four months, and the remaining 27, for from three weeks to three months. One hundred forty-seven, or 34%, of these records were normal, and not to be distinguished from the records which predominated for the normal subjects; 148, or 34%, were abnormal (+, ++, or +++), and 142, or 32%, were questionably normal (±).

The normal and questionably normal records have already been described. The same criteria applied to both patients and normal subjects. There were two distinct types of abnormal records. The first type (+) of abnormal record was characterized by very short, and often broad, fractions and by a decrease in the number of fractions in at least three conditions (Figs. 4 *A*, *C*, and *E*; 5*C*, and 6 *D*). This type of chromatogram was not noted in the earlier study by Swank, Franklin, and Quastel.[1] The second type (++) of abnormal record was poorly organized and contained less than the normal number of fractions in three or more conditions. Sometimes this type of chromatogram contained 10 or fewer very large fractions, usually unevenly grouped or bunched together (Fig. 3 *A*). In other (++) abnormal records there were wide gaps containing no fractions (Fig. 3 *E*). This type of abnormality was noted before by Swank, Franklin, and Quastel [1] in patients with multiple sclerosis during activity of the disease. A third type (+++) of abnormal record contained features of both the + and the ++ abnormal records (Fig. 6 *E*). Eighty-three of the 148 abnormal records were of Type +; 33, of Type ++, and 32, of Type +++.

For some patients the abnormal chromatograms were scattered indiscriminately among the normal and the questionably normal records (Fig. 7; Case 4), but usually they occurred in cycles every one to three months and lasted one to four weeks (Fig. 7; Cases 5, 6, and 7). The + abnormal records had the greatest tendency to appear periodically, but occasionally ++ or +++ abnormal records were mixed with the + abnormal records.

One patient with multiple sclerosis was studied during pregnancy. Nineteen chromatograms were made at weekly intervals. Four of these were questionably normal, and all the remaining 15 were of either the ++ or the +++ abnormal type.

Correlation of Chromatograms with Clinical Activity of Multiple Sclerosis.—In 13 cases mild fluctuations of the disease (10 cases) or exacerbation of the disease (3 cases) occurred either during a period when a series of two to five chromatograms were abnormal or within less than a week after the last of a series of abnormal chromatograms (Fig. 7; Cases 5 and 6). In one instance a fluctuation occurred without apparent relation to an abnormal chromatogram. In seven instances in which activity of the disease was noted clinically the predominating type of plasma protein abnormality was either Type ++ or Type +++ and in six cases the prevailing abnormality was Type +. It should be noted that abnormal chromatograms occurred frequently without associated clinical activity of disease.

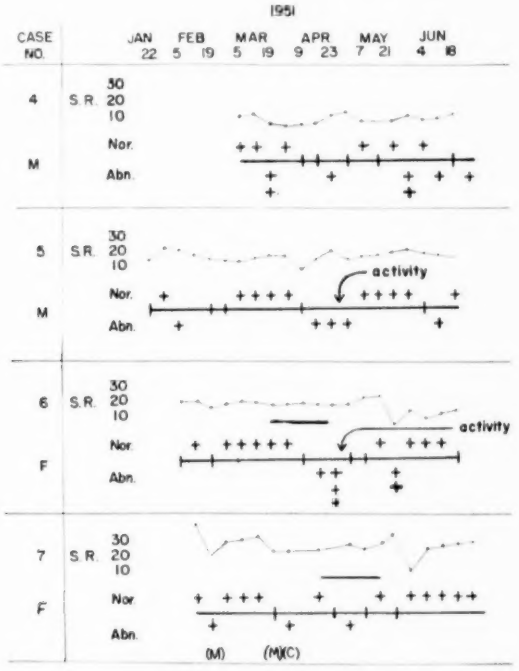

Fig. 7.—Distribution of normal, abnormal, and questionably normal chromatograms taken at weekly intervals from patients with multiple sclerosis. An explanation of the figure is given in the legend for Figure 1.

Relation of Chromatogram to Sedimentation Rate.—Sedimentation rates were determined on each blood sample, but no clear-cut relation of the sedimentation rates to changes in the plasma protein pattern was noted. The sedimentation rates are plotted in Figures 1 and 7. It was noted before [1] that the sedimentation rate was generally more rapid in patients with multiple sclerosis than in normal human subjects, and this observation was verified in the present study; but no correlation of rapid or slow sedimentation rates with normal or abnormal chromatograms was noted.

COMMENT

The studies just reported indicate that an abnormal pattern of the plasma proteins can be detected periodically by paper chromatography in patients with multiple sclerosis. Usually this abnormality recurs at intervals of one to three months and is present for a few days to about four weeks. In a few patients these abnormalities recur more frequently. In all patients with multiple sclerosis, except one woman who was pregnant, normal plasma protein patterns as measured by paper chromatography were frequently seen. A cyclic variation in the pattern of plasma proteins was detected in most of the normal subjects, but the variation in their chromatograms was less pronounced, was of shorter duration, and was almost always confined to changes within the boundaries of normality. In 13 patients with multiple sclerosis clinical activity in the form of fluctuations or clear-cut exacerbation of disease was recorded. In 12 cases this activity was concurrent with or in very close relation to the period when abnormal chromatograms were recorded. Only once was clinical activity recorded during a period when all chromatograms were normal.

In patients with multiple sclerosis the + type of abnormal chromatogram usually predominated during the cyclic departures of the plasma protein patterns from normal. The ++ type of abnormality was less frequent in occurrence and was likely to be present during periods of obvious clinical activity of the disease. This type of abnormal chromatogram was observed previously during exacerbations of disease,[1] and similar changes were observed in dogs after large fat feedings and after intravenous injections of heparin.[6] Both the + and the ++ types of abnormality were seen in normal subjects during the common cold and during the menstrual cycle. It is of interest that my colleagues and I did not note the + abnormality in the chromatogram in a previous study.[1] This was probably because the + change is less obvious than the ++ and +++ abnormalities and because it was periodic in occurrence. In our subsequent study of a much larger number of normal subjects and patients, more frequently and for a longer period, this change has become evident. It is important to note that incomplete drying of the papers between solvents may occasionally lead to shortening of the fractions, which can be misleading.

Evidence is accumulating to suggest that a defect in basic metabolism is present in multiple sclerosis and is genetically determined.[7] The observation of similar plasma protein patterns in normal sisters of patients with multiple sclerosis in the present study can be interpreted as support for this view. These and other observations in one other of our normal human subjects suggest that the abnormal plasma protein patterns, although present in all patients with multiple sclerosis which we have so far studied, are not sufficient by themselves to cause the clinical manifestations of the disease to develop. For this reason, and because so many normal records were obtained in patients, it seems unlikely that the supposed defect in basic

6. (*a*) Swank, R. L.; Franklin, A. E., and Quastel, J. H.: Effects of Fat Meals and Heparin on Blood Plasma Composition as Shown by Paper Chromatography, Proc. Soc. Exper. Biol. & Med. **75**:850-854, 1950. (*b*) It should be noted that the addition of heparin to whole blood in vitro to prevent coagulation does not alter the chromatogram from that seen when ammonium potassium oxalate is used as the anticoagulant.

7. Mackay, R. P.: Familial Occurrence of Multiple Sclerosis and Its Implications, A. Res. Nerv. & Ment. Dis., Proc. **28**:150-177, 1950. Pratt, R. T. C.; Compston, N. D., and McAlpine, D.: Familial Incidence of Disseminated Sclerosis and Its Significance, Brain **74**:191-232, 1951.

metabolism in multiple sclerosis consists of the plasma protein abnormality described in this or in a preceding paper.[1] The recurring plasma protein abnormality could be an indication of an underlying metabolic defect not yet identified, or be one of a number of factors in the disease.

At present it is not possible to state whether the + and ++ types of abnormal chromatograms represent related plasma protein changes or are totally unrelated, and whether the changes observed during the common cold, during menstruation, during pregnancy, and occasionally in normal subjects are related to the plasma protein abnormalities seen in patients with multiple sclerosis. It can be speculated that the abnormal chromatograms represent plasma protein deficits which render the patient vulnerable to factors capable of precipitating attacks of the disease. It has already been suggested [8] that a high-fat diet is an important precipitating factor in this disease, and it is significant that high-fat feedings produced plasma protein patterns in dogs [6a] similar to the type of defect most commonly associated in our patients with clinical activity of the disease.[1] It has been shown that high-fat feedings [9] alter the suspension stability of the blood, and the means by which this change could cause demyelination in the central nervous system has been discussed in other papers.[10] It is of interest that intravenous injections of heparin produce similar changes in the plasma protein patterns in paper chromatography [6a] and, as well, an alteration in the suspension stability of the blood [9] visible in dark-field preparations. The possibility that multiple sclerosis may be precipitated by an allergic reaction (McAlpine and Compston [11]; Ehrentheil and associates [12]), and the fact that heparin is liberated into the circulation during anaphylactic shock open avenues for speculation as to the possible common mechanisms by which allergens and a high-fat intake may produce the neurologic lesions seen in multiple sclerosis.[3]

It can be speculated further that the + abnormality in paper chromatograms represents a causal or predisposing factor in multiple sclerosis, whereas the ++ abnormality represents a nonspecific change which has been associated with or resulted from activity of the disease. One can carry this speculation no further, since there is no way of knowing whether the changes in pattern of the plasma proteins are due to the presence of abnormal fractions or to a deficiency of protein fractions, or are due to alterations in protein or nonprotein substances which influence the distribution of the plasma protein fractions in the paper chromatogram. At the moment the latter explanation seems more likely.

---

8. Swank, R. L.: Multiple Sclerosis: A Correlation of Its Incidence with Dietary Fat, Am. J. M. Sc. **220**:421-430, 1950. Swank, R. L.; Lerstad, O.; Strøm, A., and Backer, J.: Multiple Sclerosis in Rural Norway: Its Geographic and Occupational Incidence in Relation to Nutrition, New England J. Med. **246**:721-728, 1952. Swank.[3]

9. (*a*) Swank, R. L.: Changes in Blood Produced by a Fat Meal and by Intravenous Heparin, Am. J. Physiol. **164**:798-811, 1951. (*b*) It has recently been demonstrated (R. L. Swank and S. T. Cullen) that high-fat feedings significantly alter the suspension stability of the circulatory blood in the cheek pouch of the hamster. A report of this study will appear in the *Proceedings for the Society of Experimental Biology and Medicine.*

10. (*a*) Swank, R. L., and Hain, R. F.: Effect of Different-Sized Emboli on the Vascular System and Parenchyma of the Brain, J. Neuropath. & Exper. Neurol. **11**:280-299, 1952. (*b*) Swank.[3]

11. McAlpine, D., and Compston, N.: Some Aspects of the Natural History of Disseminated Sclerosis, Quart. J. Med. **21**:135-167, 1952.

12. Ehrentheil, O. F.; Shulman, M. H., and Alexander, L.: Role of Food Allergy in Multiple Sclerosis, Neurology **2**:412-426, 1952.

Before paper chromatography can be helpful in the diagnosis of multiple sclerosis, many more disease conditions will have to be studied intensively. At present many weekly samples of blood must be studied to determine the over-all pattern of the plasma proteins, and this limits the usefulness of chromatography as a test for the disease. The method may prove of value, however, in following the activity of the disease during therapy. Since many of our patients were on a low-fat diet, it is possible that the basic pattern had already been altered. This is doubtful, since both patients and normal subjects were studied on normal diets and on low-fat diets.[1] One might anticipate that the elimination of precipitating factors of the disease, e. g., a high-fat intake, would influence the chromatogram very little, whereas elimination of basic metabolism factors would prevent the cyclic departure of the plasma protein patterns from normal.

SUMMARY AND CONCLUSIONS

The plasma proteins of 21 normal subjects and of 41 patients with multiple sclerosis were studied at weekly intervals over periods ranging from a few weeks to five months. Two hundred forty-three chromatograms from normal subjects and 437 chromatograms from patients with multiple sclerosis were satisfactory technically and form the basis for the present report.

A high incidence of abnormal patterns in the chromatograms was observed for the patients with multiple sclerosis. They tended to recur in cycles every one to three months and to be present for periods of one to four or five weeks. Sometimes the abnormalities in the plasma protein pattern occurred more frequently and for shorter periods. In 13 instances clinical activity of the disease was noted. In 12 of these the activity was concurrent with, or in close association with, the periods when the chromatograms were abnormal. Oftener, however, the abnormal chromatograms were not accompanied by clinical activity of the disease.

A cyclic change in the plasma protein chromatograms also occurred in normal subjects, but these variations were not marked and lasted for only short periods. During the common cold and during menstruation the chromatograms tended to be abnormal, and for one normal subject and for two normal sisters of patients abnormal chromatograms were frequently seen.

EFFECT OF PREFRONTAL LOBOTOMY ON INTELLECTUAL FUNCTIONING IN CHRONIC SCHIZOPHRENIA

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ONE OF the basic questions in an evaluation of prefrontal lobotomy is its effect on the intellectual functions in man. There is present in the literature a vast amount of material on this general problem, but, despite the quantity, there is little agreement on the fundamental points. Even on the basis of objective tests an evaluation of prefrontal lobotomy is complicated by conflicting results.

From their investigations, Malmo,[1] Petrie,[2] Yacorzynski and associates,[3] and Rylander [4] reported a loss in intelligence test scores, while no gross decrease was noted in the studies done by Frank,[5] Hunt,[6] McKenzie and Proctor,[7] and Robinson.[8] On the other hand, Carscallen and associates [9] and Oltman and associates [10] stated that there is a general rise in intellectual functioning above the preoperative level, whereas the Columbia Greystone Study,[11] Hebb,[12] and Lidz [13] observed no significant differences.

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5. Frank, J.: Clinical Survey and Results of 200 Cases of Prefrontal Leucotomy, J. Ment. Sc. **92**:497-508, 1946.

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(Footnotes continued on next page)

Differences in clinical approach, operative procedure, and selection of patients; conclusions based on small groups or on isolated cases; the absence of adequate control groups or preoperative records for use as a comparative standard; the importance of the time element and the difference of opinion about the concept "intelligence" may in part account for the apparently discordant claims and results.

THE PROBLEM

The primary purpose of this study was to evaluate the effect of prefrontal lobotomy upon intellectual functioning as measured by a battery of psychological tests. A comparison of the postoperative scores with those obtained prior to operation should indicate to what extent intellectual functioning is affected by the operation. The relation of the time intervals of testing to the loss or gain in intellectual function should become apparent. By utilization of psychological tests of intelligence and memory, two aspects of intellectual functioning were observed. The effect of prefrontal lobotomy on intelligence should be clarified further by a comparison of test results obtained before and after the patients became psychotic.

MATERIAL AND METHODS

The Design.—A battery of seven psychological tests was administered prior to operation and at intervals of three weeks, three months, six months, and one year after operation. Only four of the tests selected were of the standarized type which would lend themselves to a quantitative analysis. Therefore, this study is limited to the results obtained from the Wechsler-Bellevue Intelligence Scale, the Wechsler Memory Scale, the Benton Visual Retention test, and Raven's Progressive Matrices.[14]

As would be expected in a study dealing with psychotic patients, the number of usable test results was considerably decreased, since the obtaining of such results depends to a large extent on the accessibility and availability of the patients. The only test results used were those of 26 male schizophrenic patients with complete preoperative and postoperative test records, i. e., complete test batteries obtained before the operation and for intervals of three weeks, three months, six months, and a year after the operation. These records were felt to represent the best efforts of a cooperative patient. Table 1 presents the composition of the group finally selected for this study.

All the lobotomized patients were from the general psychiatric wards of Westminster Hospital. In each case prefrontal lobotomy was considered as a "last-resort" therapy, administered only when other forms of treatment during the earlier phases of the illness produced no improvement.

The candidates were taken to Sunnybrook Hospital, Toronto, where the standard type of prefrontal lobotomy was performed by Dr. E. H. Botterell. The technique used was that of a superior open approach.

The retraining program of the postoperative patients was one of "total push," under the supervision of a relatively constant staff in a ward that was separate and distinct from other treatment groups.

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11. King, H. E.: Intellectual Functions, in Selective Partial Ablation of the Frontal Cortex: Its Effect on Human Psychotic Subjects, edited by F. A. Mettler, New York, Paul B. Hoeber, Inc., 1949, pp. 178-207.

12. Hebb, D. O., and Penfield, W.: Human Behavior After Extensive Bilateral Removal from the Frontal Lobes, Arch. Neurol. & Psychiat. **44**:421-438, 1940.

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14. The other psychological tests used were the Rorschach, the Thematic Apperception test, and the Shaw Blocks.

The Control Group.— The need for a control group was readily recognized by the investigators, and such a group was set up in conjunction with the lobotomy research program. This group followed the same daily routine and psychological testing schedule as did the lobotomy patients. However, by the third postoperative month the control group was discontinued because seven of the patients became so overtly disturbed that they were returned to the closed wards, one was discharged from the hospital, and another became a candidate for lobotomy.

TABLE 1.—*Variables in Group of Male Lobotomy Patients Utilized in Present Study*

No. of patients	26
Psychiatric diagnosis, no. of patients	
Paranoid schizophrenia	20
Catatonic schizophrenia	2
Simple schizophrenia	2
Unclassified schizophrenia	2
Age	
Average, yr.	34.6
Range, yr.	24-50
Length of illness	
Average, yr.	4.27
Range, yr.	1.4-8
Wechsler-Bellevue full-scale I. Q.	
Preoperative average	94.5
Preoperative range	62-130

TABLE 2.—*Significance of Differences Between Preoperative and Postoperative Scores for Lobotomy Patients on Wechsler-Bellevue Intelligence Scale*

	A	B	C	D
1. Full Scale				
N = 26				
Mean difference	− 5.96	+ .923	+ 6.04	+ 5.46
σ diff.	3.18	2.07	2.56	2.77
t value	1.87	0.446	2.36*	1.97
2. Verbal Scale				
N = 26				
Mean difference	− 6.62	− 2.27	+ 1.23	− 1.54
σ diff.	3.46	2.44	2.73	2.73
t value	1.19	0.930	0.451	0.564
3. Performance Scale				
N = 26				
Mean difference	− 4.31	+ 4.69	+10.81	+13.22
σ diff.	2.98	2.53	3.27	3.84
t value	1.45	1.85	3.31†	3.44†

* For significance at the 0.05 level, $t = 2.064$.
† For significance at the 0.01 level, $t = 2.797$.

RESULTS

In analysis of the results of the four psychological tests, the postoperative scores were compared with the preoperative scores at successive intervals of three weeks, three months, six months, and one year to determine whether any statistically significant differences occurred in the mean scores at any of these periods. Differences between the preoperative test scores and the scores at three weeks after the

operation are labeled A; in like manner, differences between the preoperative test scores and the postoperative scores obtained at the three-month, six-month, and one-year intervals are labeled B, C, and D respectively.

The statistical results for the Wechsler-Bellevue Intelligence Scale are based on the total group of 26 lobotomy patients. However, only 23 records were retained for the Wechsler Memory Scale and 22 each for the Benton Visual Retention test and the Progressive Matrices test, since there were no preoperative results because of such factors as inaccessibility, lack of cooperation, or acute hostility.

The Wechsler-Bellevue Intelligence Scale.—Table 2 presents the mean differences and *t* values for the 26 lobotomized patients. For added clarity, the results have been derived from the full, verbal, and performance scales of the Wechsler-Bellevue test.

Of the 12 differences, 1 is significant at the 0.05 level of confidence, and 2 are significant at the 0.01 level of confidence. It is of particular interest to note that both the differences that are very significant appear at the six-month (C) and one-

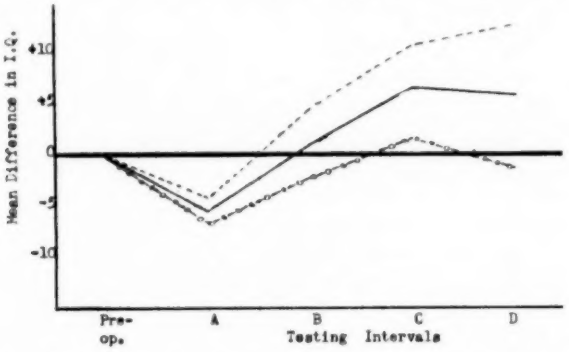

Fig. 1.—Mean differences in total scores obtained by the lobotomy patients on successive tests of the Wechsler-Bellevue Intelligence Scale. Full-scale scores are indicated by the solid line; for the verbal scale, scores by the line of circles, and for the performance scale, scores by the broken line.

year (D) comparisons on the performance scale, thus suggesting that the lobotomy patients do better after than before operation on the performance items. The full-scale scores, which are additive results of the verbal and performance results, do not show any significant difference until the six-month (C) interval, when they are significant at the 0.05 level.

These results are graphically presented in Chart 1, by plotting the mean differences on a scale in which the abscissae are the successive postoperative testing intervals. For comparison, the preoperative level is indicated by a heavy line at ordinate 0, parallel to the X axis.

It would appear from these results that there is a slight decrease in intelligence, as obtained on the Wechsler-Bellevue Intelligence Scale, three weeks (*A*) after the operation, followed by an increase at three months (*B*). At the six-month interval (*C*) the intelligence quotient has risen slightly above the preoperative level of intelligence. The fourth postoperative testing (*D*) shows a slight decline in the verbal and full-scale scores, despite the significant continued increase in the performance scale.

Since the time of administration seems to be of great importance, as may be inferred from Chart 1, an analysis of variance [15] was computed to determine its statistical significance.

It may be seen from Table 4 that the various types of tests here used do not differ significantly in their effect on the intelligence quotient scores, that the interaction between the test and the time of its administration is significant only at the 0.05 level, but that the time of its administration has a decidedly significant effect on test performance.

TABLE 3.—*Analysis of Variance*

N = 26 Source	Sum of Squares	Degrees of Freedom (*d. f.*)	Variance Estimate
Rows { Full scale, Verbal scale, Performance scale }	315.80	2	157.9
Columns (time)	7,199.78	4	1,799.94
Interaction	1,794.63	8	224.33
Within cells	86,190.58	765	112.67
Total	95,500.79	779	

TABLE 4.—*Variance Ratios (F) and Their Significance*

	Analysis of Variance Ratios (*F*)	Degree of Freedom (*d. f.*)		Significance	
		N_1	N_2	*P* 0.05	*P* 0.01
Full, Verbal, Performance scales	1.40	2	765	3.00	4.64
Time	15.67	4	765	2.38	3.35
Interaction	1.90	8	765	1.95	2.54

TABLE 5.—*Significance of Differences Between Preoperative and Postoperative Scores for Lobotomy Patients on Raven's Progressive Matrices Test*

N = 22	A	B	C	D
Mean differences	− 3.42	− 1.18	− 0.68	+ 1.41
σ diff	2.15	2.30	2.32	2.50
t value	1.59	0.513	0.289	0.564

* For significance at 0.05 level, $t = 2.080$.

The Progressive Matrices.—Table 5 summarizes the statistics for 22 lobotomy patients on Raven's Progressive Matrices. None of the four differences show any statistical significance on this nonverbal test of intelligence. The loss in test scores is most apparent at the three-week level (*A*), where it approaches the 0.05 level of significance.

The slow increase in test scores is shown by Chart 2. The loss three weeks after the operation (*A*) is slowly regained, until at the one-year level (*D*) the scores have exceeded those obtained prior to operation.

15. Miss Doreen Carruthers, of the University of Western Ontario, made the statistical computations in Tables 3 and 4.

The Wechsler Memory Scale.—The mean differences and *t* ratios for 23 lobotomy patients obtained on the Wechsler Memory Scale are shown in Table 6. There is nothing of statistical significance until the six-month (*C*) period, when the difference is significant at the 0.05 level of confidence. Chart 3 presents the graphic representation of these data. It is interesting to note that the Wechsler Memory Scale appears to show no loss when compared with the preoperative scores.

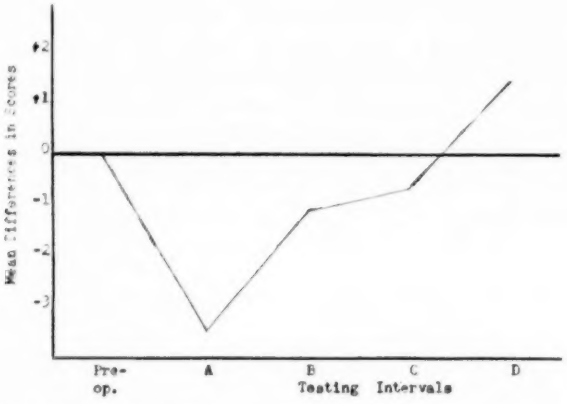

Fig. 2.—Mean differences in total scores obtained by 22 lobotomy patients on successive tests of the Raven Progressive Matrices.

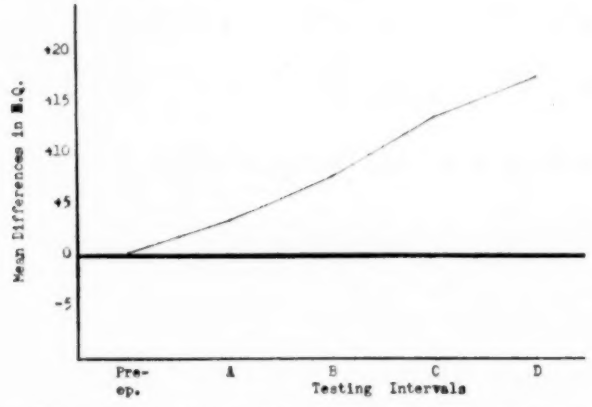

Fig. 3.—Mean differences in total scores obtained by 23 lobotomy patients on successive tests of the Wechsler Memory Scale.

TABLE 6.—*Significance of Differences Between Preoperative Scores for Lobotomy Patient on Wechsler Memory Scale*

N = 23	A	B	C	D
Mean differences	+ 3.05	+ 7.96	+13.70	+17.04
σ diff.	3.84	4.86	5.45	8.46
t value	0.843	1.64	2.51*	2.01

* For significance at the 0.05 level, $t = 2.074$.

The Benton Visual Retention Test.—The results of 22 lobotomy patients on the Benton Visual Retention test are given in summarized form in Table 7. Although none of the scores show any statistically significant difference, a significance at the 0.05 level of confidence is approached at the three-week period (*A*). A graphic representation of these results is given in Chart 4.

Spearman's rank-difference method was used in correlating the scores of the four psychological tests, the results of which are presented in Table 8. Test results obtained before operation and at the four postoperative periods were correlated. Similarly, correlations were derived from each test at every period with the same test at the preceding period.

TABLE 7.—*Significance of Differences Between Preoperative and Postoperative Scores for Lobotomy Patients on Benton Visual Retention Test*

N = 22	A	B	C	D
Mean differences	−0.571	+0.318	+0.091	+0.247
σ diff	0.407	0.325	0.360	0.369
t value	1.400	0.975	0.253	0.708

* For significance at 0.05 level, $t = 2.080$.

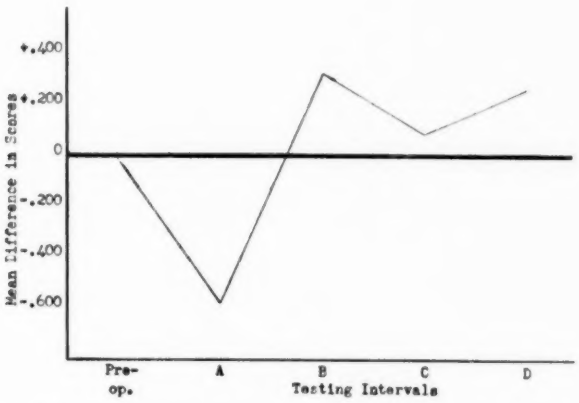

Fig. 4.—Mean differences in total scores obtained by 22 lobotomy patients on successive tests of the Boston Visual Retention test.

The reliabilities of the various tests may be seen in Table 8. It is obvious that the Wechsler-Bellevue Intelligence Scale has the highest reliability and that the Progressive Matrices test and the Wechsler Memory Scale are of fair reliability. On the other hand, the Benton Visual Retention test has reliabilities that are so low that the test is useless for prediction purposes. In a sense these intercorrelations give a clue to the degree of integration in the mental processes of the patients. To the extent that the subject maintains his efficiency on a test, as measured by the intercorrelations, may we infer his integration. From this standpoint, therefore, the correlations of the Wechsler-Bellevue Intelligence Scale show a diminished integration at the three-week period and a good recovery at subsequent periods. As one might expect, the Progressive Matrices test and the Wechsler Memory

Scale show a progressive diminution of the correlations with increasing length of time between the preoperative and the postoperative tests; yet, in general, the correlations of these successive test scores are of fair reliability.

COMPARISON OF INTELLIGENCE TEST RESULTS IN NONPSYCHOTIC AND IN PSYCHOTIC SUBJECTS

In order to study further the effect of prefrontal lobotomy on intelligence, we obtained the Army M test scores for 11 of the 26 patients used in this study. The "group equivalents" of the M test and the Wechsler-Bellevue Intelligence Scale were made available by Dr. H. E. Rosvold. Accordingly, prorated equivalent Wechsler-Bellevue intelligence quotients were assigned the M test scores. The mean differences and t values of the prelobotomy and postlobotomy Wechsler-Bellevue scores are compared with the premorbid levels of intelligence (Army M scores) in Table 9.

TABLE 8.—*Correlations of Tests*

	Postoperative Intervals			
	1st	2d	3d	4th
Wechsler-Bellevue Intelligence Scale				
Preoperative	0.63	0.77	0.77	0.71
Successive tests	0.63	0.86	0.92	0.80
Progressive Matrices test				
Preoperative	0.79	0.71	0.49	0.53
Successive tests	0.79	0.73	0.71	0.83
Wechsler Memory Scale				
Preoperative	0.70	0.42	0.43	0.17
Successive tests	0.70	0.28	0.71	0.70
Benton Visual Retention test				
Preoperative	0.38	0.53	0.40	0.30
Successive tests	0.38	0.39	0.39	0.49

TABLE 9.—*Significance of Differences Between Preoperative and Postoperative Scores on Wechsler-Bellevue Test and Army M Test*

		Postoperative			
N = 11	Pre-operative	3 Wk.	3 Mo.	6 Mo.	1 Yr.
Mean differences	−12.09	−17.63	− 9.45	− 4.00	− 3.63
σ diff.	5.08	4.40	3.73	3.05	3.34
t value	2.38*	4.01†	2.53*	1.31	1.09

* For significance at the 0.05 level, $t = 2.262$.
† For significance at the 0.01 level, $t = 3.250$.

Of the five differences presented, three are statistically significant. When the preoperative intelligence quotients were compared with those obtained before the patients became mentally ill, a significant difference was indicated at the 0.05 level of confidence. A very significant difference was noted three weeks after the operation and a less significant difference at the three-month period of testing. Chart 5 presents a graphic representation of these results. In this figure the premorbid score was taken as the base line from which differences were computed.

It is suggested from these results that significant differences in intelligence quotients occur before and three months after operation. The most significant difference

occurs three weeks after the operation, a finding in accordance with the results obtained for the total group. At the six-month and one-year postoperative testing the differences are much less, suggesting that the loss in intelligence is slowly being regained. It is important, then, to keep in mind these changes, as well as those obtained three months after the operation. These data, then, indicate that after lobotomy the level of intelligence was changed from that measured while the patients were psychotic, a result which is in disagreement with that obtained in a study by Rosvold and Mishkin.[16]

Thus, when the intelligence of psychotic patients was compared with their premorbid intelligence, impairment was demonstrated. But when the study was carried over a sufficient length of time, a gradual increase in the intellectual functioning was noted, the intelligence surpassing the preoperative level and with a tendency to reach

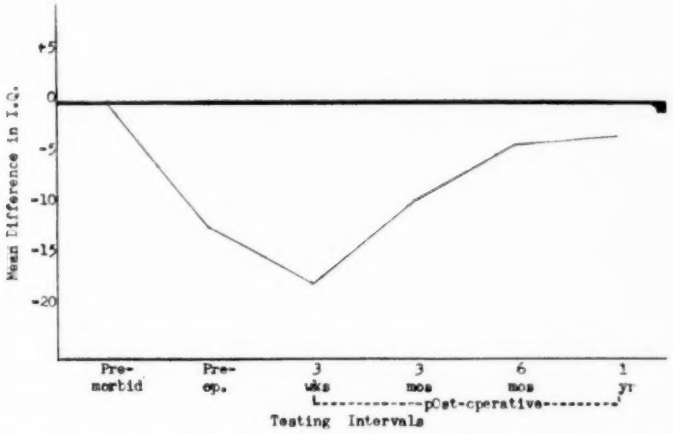

Fig. 5.—Mean differences in total scores obtained by 11 lobotomy patients on the Army M test and successive tests of the Wechsler-Bellevue Intelligence Scale.

TABLE 10.—*Premorbid, Preoperative, and Postoperative Scores Obtained by Eleven Lobotomy Patients on the Wechsler-Bellevue and Army M Tests*

Patient No.	Army M Score	W-B Group Equivalent	Prorated W-B I. Q.	Pre-operative I. Q.	Postoperative I. Q. (1) 3 Wk.	(2) 3 Mo.	(3) 6 Mo.	(4) 1 Yr.
1	101	80-90	84	93	79	88	94	99
2	119	90-110	93	94	82	92	97	97
3	104	90-110	97	67	90	88	101	98
7	101	80-90	84	74	71	81	80	80
8	143	110-120	112	88	89	94	104	99
9	147	110-120	114	110	96	114	120	125
10	155	110-120	117	80	79	84	92	104
12	117	90-110	92	62	72	78	79	71
14	114	80-90	90	103	54	77	84	86
15	134	90-110	105	87	72	81	94	91
25	91	80-90	80	77	90	87	79	78

16. Rosvold, H. E., and Mishkin, M.: Evaluation of the Effects of Prefrontal Lobotomy on Intelligence, Canad. J. Psychol. **4**:122-126, 1950.

the premorbid level. Whether the slight deficit in intelligence still present at the one-year postoperative testing is a result of the lobotomy or of the possible deteriorating influence of the psychosis remains a problem for further investigation.

COMMENT

The Wechsler-Bellevue Intelligence Scale, Raven's Progressive Matrices, the Wechsler Memory Scale, and the Benton Visual Retention test were used to study the effects of prefrontal lobotomy on intellectual functioning in a group of 26 patients with chronic schizophrenia. When the scores obtained at successive intervals of three weeks, three months, six months and one year after operation were compared, an indication of the gains or losses was demonstrated at each period.

The results indicated no gross permanent deficit in intelligence or memory. There was a decrease in intellectual functioning at the three-week postoperative period, but it was followed by a gradual increase in intellectual functioning on successive testing intervals, so that at least the preoperative level was attained.

The most important finding in this study is the significance of the time factor in testing intervals. Three weeks after the operation a decrease in intellectual functioning is apparent, but it is followed by a gradual increase until by the six-month period the level of intellectual functioning has risen to equal, if not surpass, the preoperative level. Moreover, further increases in intellectual functioning are demonstrated at the one-year period. These results become apparent only when a study has been carried on for a sufficient length of time. It would appear that investigators who report a decrease in intellectual functioning have made their conclusions too hastily. At three weeks, and even at three months, the residual organic overlay of the operation may be clouding the results. In view of this possibility, it would seem necessary to continue any investigation of the effects on intellectual functioning for at least one year after the lobotomy; and any conclusions made before a sufficient period had elapsed after the operation would only be misleading, and probably false.

The question as to why the intelligence of these lobotomy patients showed an increase after operation is pertinent to the discussion. Since the nature of this study required the administration of the tests before operation and successive repetitions afterward, it might be expected that most patients would show an improvement arising from the practice effect. Unfortunately, no control group was available with which to compare this variable. However, in the Columbia-Greystone Study, in which a control group was utilized, the authors stated [17]:

> There was a consistent tendency for the control group to show a greater gain in score on retesting than was exhibited by the operatee group. This discrepancy between the groups was generally greater at R1 [retest at 3 weeks after the operation] but clearly present on both R1 and R2 [retest at 4 months after the operation] . . . . Since practice effects are to be expected on repetition of a test, it would seem that the operatee group was not able to profit from its previous experience with the test to as great an extent as were the controls. Another possible explanation could be that an actual loss in ability has occurred but there has been no interference with practice effect, and that this serves to mask the actual loss. . . . It would appear unlikely that such a "loss" on each test would be so neatly covered by the practice effect.

Clearly, the effects of practice cannot be disputed on the basis of the present data, but whether practice would account for the significant gains remains problematical.

17. King,[11] p. 204.

It might be expected that the lobotomized patients would make scores greater on verbal items, where they have an opportunity to familiarize themselves with the correct responses. However, this was not the case, as demonstrated by the consistently higher scores on the performance scale of the Wechsler-Bellevue Intelligence Scale. Furthermore, after the operation there seems to be a tendency on the part of the patient to be more cooperative and pleasant, a change which may, in part, suggest an explanation for the increase in intellectual functioning.

Another consideration is the questionable effect of the program of "total push" on the postlobotomy patient and, inadvertently, on his intellectual functioning. The very fact that the control group was discontinued because 7 of the 11 patients had to be returned to closed wards, even though they were on the same daily routine and planned program as the lobotomy group, suggests that the increase in intellectual functioning was not affected very much, if at all, by this program.

In the selection of patients for lobotomy, chronicity and length of illness were stressed, so that the operation was considered a "last-resort" therapy. The possibility of intellectual deterioration caused by the psychosis cannot be ignored. From this study it is suggested that any loss in intellectual functioning following prefrontal lobotomy may be due not to the operation but, rather, to the effect of the psychosis.

The evidence obtained from this study is in agreement with the results of some investigators and in opposition to the observations of others. The general absence of measurable loss in intelligence following prefrontal lobotomy is in agreement with the reports of Frank, Hunt, McKenzie, Robinson, and Carscallen and associates, with the results of lobectomy studies done by Hebb [18] and Lidz, and with the findings in the topectomy studies of the Columbia-Greystone associates, reported by King. The results did not reflect the decrease in intelligence noted by Malmo, Petrie, and Yacorzynski and associates following lobotomy or in the lobectomy cases studied by Rylander. The present study most closely resembles that reported by Oltman and associates in respect to surgical approach, subject make-up, and the general results obtained from similar psychometric tests. Furthermore, the results obtained one year after the operation provide further support for the conclusions drawn by Carscallen in a preliminary study in which the present 26 patients were included.

SUMMARY AND CONCLUSIONS

The Wechsler-Bellevue Intelligence Scale, Raven's Progressive Matrices, the Wechsler Memory Scale, and the Benton Visual Retention test were used to study the effects of prefrontal lobotomy on intellectual functioning in a group of patients with chronic schizophrenia. By comparison of the scores obtained prior to operation with those obtained at successive intervals of three weeks, three months, six months, and one year after operation, an indication of the gains or losses in intellectual functioning was demonstrated at each period. After the operation all the four tests showed the same general increase in intelligence.

The most important finding in this study is the significance of the time factor in testing intervals. Three weeks after the operation a decrease in intellectual functioning was apparent, but it was followed by a gradual increase, until by the six-month period the intellectual functioning had arisen to equal, if not surpass

18. Hebb, D. O.: Man's Frontal Lobes: A Critical Review, Arch. Neurol. & Psychiat. **54**:10-24, 1945.

the preoperative level. Moreover, further increases in intellectual functioning were demonstrated at the one-year period. This would suggest that any conclusions made before a sufficient period had elapsed after the operation would only be misleading, and probably false.

When the intelligence of psychotic patients was compared with their premorbid intelligence, impairment was exhibited. But when the study was continued over a sufficient length of time, a gradual increase in intellectual functioning was noted, the intelligence exceeding the preoperative level at least, and with a tendency to equal the premorbid level. It may be suggested, then, that the deficit in intelligence is not due entirely to prefrontal lobotomy, but may be caused in part by the deteriorating effect of the psychosis.

On the evidence presently available, it would be presumptuous and imprudent to conclude that prefrontal lobotomy has no effect on intellectual functioning, but it can be stated that after the lapse of six months no adverse effects on intellectual functioning were demonstrated by the objective psychometric measures utilized in this study.

AGENESIS OF THE CORPUS CALLOSUM DIAGNOSED DURING LIFE

Review of the Literature and Presentation of Two Cases

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THE INTRODUCTION of pneumoencephalography and ventriculography by Dandy [1] provided diagnostic tools for the demonstration and localization of intracranial pathology without equal in neurology, though many neurologists and neurosurgeons feel their position is currently challenged by cerebral angiography.[2] Although originally conceived as aids to the diagnosis and localization of intracranial neoplasms, a purpose nobly fulfilled, these methods have made possible the detection of numerous other intracranial conditions previously diagnosed only at operation or autopsy. The latter situation pertained particularly to the diagnosis of agenesis of the corpus callosum. In 1922 Mingazzini [3] summarized the clinicopathologic literature of agenesis of the corpus callosum and found 71 cases, in 43 of which the agenesis was complete; Baker and Graves,[4] in 1933, found a total of 82 cases and added 1 of their own. In none of these cases was the diagnosis made during life. As far as can be determined, Guttmann [5] performed the first encephalographic study on a patient with this condition but failed to make the diagnosis during life. Death occurred 14 hours after the procedure, and autopsy revealed complete agenesis of the corpus callosum, septum pellucidum, and hippocampal commissure, as well as microgyria, heterotopic occipital cortex, and anomalous development of the cere-

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1. Dandy, W. E.: Ventriculography Following the Injection of Air into the Cerebral Ventricles, Ann. Surg. **68**:5-11 (July) 1918; Ventriculography Following the Injection of Air into the Cerebral Ventricles, Am. J. Roentgenol. **6**:26-36 (Jan.) 1919; Roentgenography of the Brain After the Injection of Air into the Spinal Canal, Ann. Surg. **70**:397-403 (Oct.) 1919.

2. Davidoff, L. M., and Epstein, B. S.: The Abnormal Pneumoencephalogram, Philadelphia, Lea & Febiger, 1950.

3. Mingazzini, G.: Der Balken: Eine anatomische, physiopathologische und klinische Studie, Berlin, Springer-Verlag, 1922.

4. Baker, R. C., and Graves, G. O.: Partial Agenesis of the Corpus Callosum, Arch. Neurol. & Psychiat. **29**:1054-1065 (May) 1933.

5. Guttmann, L.: Über einen Fall von Entwicklungsstörung des Gross- und Kleinhirns mit Balkenmangel, Psychiat.-neurol. Wchnschr. **31**:453-455 (Sept. 4) 1929.

bellum. A review of the encephalogram disclosed characteristic features, which, in retrospect, might have established the diagnosis. The first intravitam diagnoses of this anomaly were made in 1934 by Davidoff and Dyke [6] and Penfield and Hyndman.[7] Originally the encephalograms were interpreted as indicating cysts of the cavum septi pellucidi, but operation and/or autopsy ultimately revealed the true pathology. Encephalographic data obtained from the cases reported by these authors made possible the diagnosis in subsequent cases during life. A review of the literature revealed 43 cases in which the diagnosis of agenesis of the corpus callosum was made during life (Table 1).

The infrequency with which this anomaly is encountered by roentgenologists, neurologists, and neurosurgeons is demonstrated by the following: Davidoff and Dyke found 3 cases among 1,100 encephalograms made at the Neurological Institute of New York; Mäurer [8] discovered only 1 case among 1,670 encephalograms made at the Psychiatrischen und Nervenklinik der Universität Bonn prior to 1940; Krüger [9] encountered only 2 cases in all the encephalographic studies performed at the Nervenklinik der Charité prior to 1939, and Pospiech [10] found but 3 cases among 1,000 encephalographic studies done at the Landesanstalt Görden.

Since no extensive review of the literature of agenesis of the corpus callosum diagnosed during life has been made, it seemed worth while to collect the available data and report two additional cases.

REVIEW OF LITERATURE

Development of Corpus Callosum.—The corpus callosum, anterior commissure, psalterium, and septum pellucidum are thought to be derived from a slight thickening of the lamina terminalis—the so-called Hochstetter commissural plate.[11] As development takes place, there are a fusion of the two plates in the midline (raphe of the corpus callosum) and extension posteriorly over the fornices and thalami. The plate thus formed provides a conduction tissue facilitating the crossing of interhemispheric fibers.[12] Dorsal condensation of such fibers forms the corpus callosum (neopallial commissure), and ventral condensation forms elements of the anterior commissure; remnants of the commissural plate carried posteriorly beneath the corpus callosum remain as the septum pellucidum. The septa of the two sides may be fully or partially fused, leaving an interseptal space, designated as the cavum

6. Davidoff, L. M., and Dyke, G. A.: Agenesis of the Corpus Callosum: Diagnosis by Encephalography; Report of 3 Cases, Am. J. Roentgenol. **32**:1-10 (July) 1934.

7. Penfield, W., and Hyndman, O. R.: Agenesis of the Corpus Callosum, with Discussion of Ventriculograms in 2 Living Cases, Tr. Am. Neurol. A. **60**:182-184, 1934.

8. Mäurer, H.: Zur encephalographischen Diagnose des Balkenmangels, Nervenarzt **13**:454-460 (Oct.) 1940.

9. Krüger, W.: Über Balkenmangel (Balkenagenesie): Bericht über zwei eigene Fälle mit Encephalogramen, Arch. Psychiat. **110**:638-651 (Nov.) 1939.

10. Pospiech, K. H.: Encephalographische und anatomische Befunde bei angeborenem Balkenmangel und bei Erweiterungung des Cavum septi pellucidi, Ztschr. ges. Neurol. u. Psychiat. **174**:249-263 (June) 1942.

11. Hochstetter, F.: Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns, Leipzig, Franz Deuticke, 1919.

12. Marburg, O.: So-Called Agenesia of the Corpus Callosum (Callosal Defect): Anterior Cerebral Dysraphism, Arch. Neurol. & Psychiat. **61**:297-312 (March) 1949.

TABLE 1.—*Reported Cases of Agenesis of the Corpus Callosum Diagnosed by Encephalography*

Case No.	Author(s)	Date	Agenesis*			Confirmed by	
			Complete	Partial	Not Specified	Surgery	Autopsy
1	Guttmann	1929	+	..	..	..	+
	Davidoff and Dyke	1934					
2	Case 1		+	..	..	..†	+
3	Case 2		+	..	..	..	..
4	Case 3		+	..	..	..	..
	Hyndman and Penfield	1937					
5	Case 1		..	+	..	+‡	..
6	Case 2		+	..	..	+	..
7	Case 3		..	+	..	..	..
8	Case 4		+	..	..	..	..
9	Case 5		..	+	..	..	..
	Brenner	1939					
10	Case 2		+	..	..	..	..
11	Case 3		+	..	..	..	..
12	Case 4		+	..	..	..	..
13	Case 5		+	..	..	..	..
	Bannwarth	1939					
14	Case 1		+	..	..	..	..
15	Case 2		+	..	..	..	..
16	Case 3		+	..	..	..	..
17	Case 4		+	..	..	..	..
18	Case 5		+	..	..	..	..
19	Köttgen	1939	+	..	..	..	..
20	Cass and Reeves§	1939	..	+	..	..	..
	Krüger	1939					
21	Case 1		..	..	+	..	..
22	Case 2		+	..	..	..	..
23	Reeves	1939	..	..	+	..	..
24	Foerster	1939	+	..	..	+	..
25	Maurer	1940	+	..	..	..	..
26	Bannwarth	1940	+	..	..	..	..
27	Kunicki and Chorobski	1940	+	..	..	+	+
28	Gowan and Masten	1940	..	+	..	..	..
29	Goldensohn, Clardy, and Levine	1941	+	..	..	..	..
30	Derbyshire and Evans	1941	+	..	..	..	..
	Pospiech	1942					
31	Case 1		+	..	..	..	+
32	Case 2		..	+	..	..	+
33	Case 3		+	..	..	..	..
34	Palmgren and Jonsell	1942	+	..	..	..	..
35	Bunts and Chaffee	1944	+	..	..	..	..
	Echternacht and Campbell	1946					
36	Case 1		+	..	..	..	..
37	Case 2		..	+	..	..	..
38	Amyot	1948	..	..	+	..	..
39	Savitsky and Spinelli	1948	+	..	..	..	+
	Foster and Windholz	1948					
40	Case 3		+	..	..	..	..
41	Chusid, de Gutierrez-Mahoney, and Chaffee	1949	+	..	..	+	..
	Tunestam	1950					
42	Case 1		+	..	..	..	..
43	Case 2		+	..	..	..	..
44	Svatý and Mašek	1950	+	..	..	..	+
45	Sheinmel and Lawrence	1951	+	..	..	..	..

* The plus sign (+) indicates agenesis of the corpus callosum, complete, partial, or not specified, according to column, and confirmation by surgery or autopsy, according to column. Opinion as to whether the agenesis of the corpus callosum was complete or partial is ours unless otherwise stated.

† Operation was performed, but diagnosis was not established until autopsy.

‡ Diagnosis was not made at operation.

§ Cass, A. B., and Reeves, D. L.: Partial Agenesis of the Corpus Callosum: Diagnosis by Ventriculographic Examination, Arch. Surg. 39:667-681 (Oct.) 1939.

septi pellucidi.[13] Formation of these structures is usually said to begin about the third month of intrauterine life and to be completed by the fifth month.

Causes of Agenesis of Corpus Callosum.—Concepts of the etiology of agenesis of the corpus callosum are varied, although basically an arrest in development is considered the cause. Arrested development has been claimed to be due to disturbances in the closure of the anterior neuropore (de Morsier and Mozer,[14] Marchand,[15] Goldstein,[16] and Ernst[17]), disturbances of vascularization of the lamina terminalis by the anterior callosal artery (Sander,[18] Bruce,[19] and de Morsier and Mozer[14]), embryonal neoplastic formations, viz., lipoma or angioma (de Morsier and Mozer[14]), porencephaly (Kirschbaum[20]), hydrocephalus (Virchow[21]), and developmental disturbances of the commissural plate (Marburg,[12] Anton[22]). Although the precise cause of the developmental defect in any particular case is frequently impossible to determine, Bruce believed it was possible to estimate the time at which developmental arrest occurred. According to Stockard,[23] the apparent causes of the malformations are almost irrelevant, since the basic mechanism is the same, viz., local impairment of embryonal metabolism due to reduced oxygenation, increased concentrations of carbon dioxide, and interference with the supply and utilization of nutrient substances. The time at which the arrest occurs and its duration are said to be the primary determinants of the resulting anomalous formation.

Clinical Manifestations.—Although several authors have attempted to construct a clinical syndrome of the corpus callosum (Cameron,[24] Alpers and Grant,[25] Trescher

13. This space is the so-called fifth ventricle, though in normal brains it is not lined with ependyma and has no connection with the ventricular system.

14. de Morsier, G., and Mozer, J. J.: Agénésie complète de la commissure calleuse et troubles du développment de l'hémisphère gauche avec hémiparésie droite et intégrité mentale: (Le syndrome embryonnaire précoce de l'artère cérébrale antérieure), Schweiz. Arch. Neurol. u. Psychiat. **35**:317-352, 1935.

15. Marchand, F.: Über den Mangel des Balkens im menschlichen Gehirn, Klin. Wchnschr. **36**:182-183 (Feb.) 1899.

16. Goldstein, K.: Beiträge zur Entwickelungsgeschichte des menschlichen Gehirns: Vorläufige Mitteilung, Anat. Anz. **22**:415-417, 1902-1903.

17. Ernst, P.: Missbildungen des Nervensystems, in Schwalbe, E.: Die Morphologie der Missbildungen der Menschen und der Tiere, Vienna, Gustav Fischer, 1912, Vol. 2, p. 141.

18. Sander, J.: Über Balkenmangel im menschlichen Gehirn, Arch. Psychiat. **1**:128-142, 1868.

19. Bruce, A.: On the Absence of the Corpus Callosum in the Human Brain, with the Description of a New Case, Brain **12**:171-190, 1889.

20. Kirschbaum, W. R.: Agenesis of the Corpus Callosum and Associated Malformations, J. Neuropath. & Exper. Neurol. **6**:78-94 (Jan.) 1947.

21. Virchow, H.: Über ein Gehirn mit Balkenmangel, Neurol. Centralbl. **6**:263-264, 1887.

22. Anton, G.: Zur Anatomie des Balkenmangels im Grosshirn, Ztschr. allg. Heilk. **7**:53, 1886; cited by Marburg.[12]

23. Stockard, C. R.: Artificial Production of a Single Median, Cyclopean Eye in the Fish Embryo by Means of Sea Water Solution of Magnesium Chloride, Arch. Entwcklngsmechn. Organ. **24**:249-258, 1907.

24. Cameron, J. L.: The Corpus Callosum: A Morphological and Clinical Study, Canad. M. A. J. **7**:609-616 (July) 1917.

25. Alpers, B. J., and Grant, F. C.: Clinical Syndrome of the Corpus Callosum, Arch. Neurol. & Psychiat. **25**:67-86 (Jan.) 1931. Alpers, B. J.: A Note on the Mental Syndrome of Corpus Callosum Tumors, J. Nerv. & Ment. Dis. **84**:621-627 (Dec.) 1936.

and Ford,[26] Sweet[27]), clinical and experimental investigation (Dandy,[28] Van Wagenen and Herren,[29] Kennard and Watts[30]) fails to support such a thesis.

In 43 of the 45 cases collected from the literature in which encephalograms were obtained, the diagnosis was made during life. No significant sexual distribution was noted (25 males and 20 females). A history of definite birth trauma was recorded in 10 cases, while birth was said to have been normal in 25 cases. Initial symptoms became apparent shortly after birth and prior to 2 years of age in 25 cases; onset of symptoms prior to 10 years of age was recorded in 8 cases. In no cases of this series did initial symptoms appear after 20 years of age. The initial symptom was grand mal epilepsy in 18 cases, physical and/or mental retardation in 18 cases, and petit mal epilepsy in 3 cases. Other initial symptoms are recorded in Table 2. In 26 of these 45 cases grand mal seizures were reported to have occurred at some time during the period of observation. Jacksonian seizures were specifically mentioned or described in 11 cases. Combined grand mal and petit mal epilepsy was reported only once (Goldensohn, Clardy, and Levine). Criteria for the determination of retarded physical development in those cases in which it was said to have been present seemed rather loose and were not always described. Frequently cited were infant feeding problems; delay in holding the head erect, sitting, standing, and walking; retarded speech development, and delayed toilet training. Evidence of impaired mental development accompanied arrested physical development in most cases, but became apparent later. Impaired mental development without associated physical retardation was reported by Hyndman and Penfield[31] (Case 3); Goldensohn, Clardy, and Levine[32]; Bunts and Chaffee[33]; Echternacht and Campbell[34] (Case 2); Sheinmel and Lawrence,[35] and Bannwarth.[36] Retarded speech develop-

26. Trescher, J. H., and Ford, F. R.: Colloid Cyst of the Third Ventricle: Report of a Case; Operative Removal with Section of the Posterior Half of Corpus Callosum, Arch. Neurol. & Psychiat. **37**:959-973 (April) 1937.

27. Sweet, W. H.: Sleeping Intracranial Aneurysm Simulating Neoplasm: Syndrome of Corpus Callosum, Arch. Neurol. & Psychiat. **45**:86-104 (Jan.) 1941.

28. Dandy, W. E.: Congenital Cerebral Cysts of the Cavum Septi Pellucidi (Fifth Ventricle) and Cavum Vergae (Sixth Ventricle): Diagnosis and Treatment, Arch. Neurol. & Psychiat. **25**:44-66 (Jan.) 1931; Operative Experience in Cases of Pineal Tumors, Arch. Surg. **33**:19-46 (July) 1936.

29. Van Wagenen, W. P., and Herren, R. Y.: Surgical Division of Commissural Pathways in the Corpus Callosum: Relation to Spread of an Epileptic Attack, Arch. Neurol. & Psychiat. **44**:740-759 (Oct.) 1940.

30. Kennard, M. A., and Watts, J.: Effect of Section of the Corpus Callosum on the Motor Performance of Monkeys, J. Nerv. & Ment. Dis. **79**:159-169 (Feb.) 1934.

31. Hyndman, O. R., and Penfield, W.: Agenesis of the Corpus Callosum: Its Recognition by Ventriculography, Arch. Neurol. & Psychiat. **37**:1251-1270 (June) 1937.

32. Goldensohn, L. N.; Clardy, E. R., and Levine, K.: Agenesis of the Corpus Callosum: Report of Case with Neuropsychiatric, Psychologic, Electroencephalographic, and Pneumoencephalographic Studies, J. Nerv. & Ment. Dis. **93**:567-580 (May) 1941.

33. Bunts, A. T., and Chaffee, J. S.: Agenesis of the Corpus Callosum with Possible Porencephaly: Review of the Literature and Report of a Case, Arch. Neurol. & Psychiat. **51**:35-53 (Jan.) 1944.

34. Echternacht, A. P., and Campbell, J. A.: Midline Anomalies of the Brain: Their Diagnosis by Pneumoencephalography, Radiology **46**:119-131 (Feb.) 1946.

35. Sheinmel, A., and Lawrence, L. R.: Agenesis of the Corpus Callosum: Lipoma of the Corpus Callosum; Their Roentgen Recognition and Differentiation, Radiology **57**:15-24 (July) 1951.

36. Bannwarth, A.: Über den Nachweis von Gehirnmissbildungen durch das Röntgenbild und über seine klinische Bedeutung, Arch. Psychiat. **109**:805-838 (April) 1939.

TABLE 2.—*Summary of Clinical Data in Cases of Agenesis of the Corpus Callosum*

Case No.	Author	Sex	Age		Symptoms		Examination		Comment
			Onset of Symptoms	Diagnosis	Initial	Subsequent	General Physical	Neurologic	
1	Guttmann	M	Birth	5 yr.	Grand mal epilepsy (Jacksonian)	.....	Normal	Normal	Birth trauma; diagnosis made at autopsy
	Davidoff and Dyke								
2	Case 1	F	2 yr.	6 yr.	Unconsciousness; vomiting and fever	Grand mal epilepsy (Jacksonian)	Precocious puberty	Hemiparesis, left	Pneumoencephalogram at age 4; died after surgery at age 6; diagnosis made at autopsy
3	Case 2	M	14 yr.	21 yr.	Frontal headaches	Grand mal epilepsy (Jacksonian) at age 16	Normal	Left: Dysmetria; dysdiadochokinesis; homonymous quadrantic field defect; increased myotatic reflexes	.....
4	Case 3	F	2.5 yr.	3 yr.	Physical and mental retardation	Grand mal epilepsy (Jacksonian); retarded speech development	Normal	Normal	.....
	Hyndman and Penfield								
5	Case 1	M	4 yr.	8 yr.	Grand mal epilepsy (Jacksonian)	.....	Normal	Normal	Birth normal; craniotomy performed; diagnosis not made at operation
6	Case 2	F	6 mo.	18 mo.	Petit mal epilepsy	Physical and mental retardation	Normal	Normal	Birth normal; diagnosis made at operation
7	Case 3	M	19 yr.	21 yr.	Petit mal epilepsy	Mental retardation	Normal	Right hemiatrophy	Birth normal
8	Case 4	M	?	2 yr.	Physical and mental retardation	.....	Normal	Normal	Birth normal
9	Case 5	F	3.5 yr.	5 yr.	Petit mal epilepsy	.....	Normal	Normal	Birth normal
	Brenner								
10	Case 2	F	Birth	18 mo.	Physical and mental retardation	Symptoms of myxedema	Enlarged thyroid	Hypotonus; sluggish myotatic reflexes	Birth trauma
11	Case 3	F	Birth	14 mo.	Physical and mental retardation	Athetoid activity in upper extremities	Normal	Athetoid activity; hypotonus; convergent strabismus	Birth trauma
12	Case 4	F	Birth	18 mo.	Physical and mental retardation	.....	Macroglossia	Convergent strabismus	Birth trauma
13	Case 5	F	Birth	2.5 yr.	Physical and mental retardation	Unable to stand or walk	Cephalic enlargement	Amytonia	Birth trauma
	Bannwarth								
14	Case 1	M	6 mo.	28 yr.	Left hemiparesis	Physical and mental retardation; grand mal epilepsy at 18 yr.	Bilateral genu valgum; pes planus	Left hemiparesis; palsy left 3d nerve	Birth normal

15	Case 2	M	6 mo.	11 yr.	Right hemiparesis	Physical and mental retardation; grand mal epilepsy at 10 yr.	Optic atrophy	Left hemiparesis	Birth normal
16	Case 3	M	7 mo.	7 mo.	Mental retardation	.....	Brachycephaly	Bilateral spasticity	.....
17	Case 4	F	6 mo.	2 yr.	Grand mal epilepsy	Physical and mental retardation; athetoid activity	Microcephaly; macroglossia	Paraparesis with spasticity; athetoid activity	Birth trauma
18	Case 5	M	?	9 yr.	Impaired vision	Normal	Optic atrophy	Horizontal and rotary nystagmus	Birth normal
19	Köttgen	F	?	4 yr.	Physical and mental retardation	Retarded speech development	Normal	Divergent strabismus	Birth normal
20	Cass and Reeves	F	?	9 mo.	Physical and mental retardation	.....	Normal	Normal	Birth normal
	Krüger								
21	Case 1	M	?	51 yr.	Mental retardation	.....	Normal	Normal	.....
22	Case 2	M	12 yr.	20 yr.	Grand mal epilepsy (Jacksonian)	.....	Normal	Right facial paresis	Birth normal; defect surgically verified
	Reeves								
23	Case 2	F	2 mo.	6 mo.	Grand mal epilepsy (Jacksonian)	Physical and mental retardation	Coloboma left optic nerve; pigment degeneration of retina	Bilateral Babinski sign; increased intracranial pressure	Birth normal; porencephalic cyst
24	Foerster	M	18 yr.	29 yr.	Grand mal epilepsy (Jacksonian)	.....	Normal	Normal	Birth normal; paraphysial diverticulum
25	Mäurer	M	6 yr.	33 yr.	Mental retardation	Digital tremor; rigidity; impaired speech	Normal	Adiadochokinesis; tremor; rigidity	Birth normal
26	Bannwarth	M	16 yr.	27 yr.	Grand mal epilepsy	Athetoid activity	Normal	Athetoid activity; left upper extremity	Birth normal
27	Kunicki and Chorobski	M	?	21 mo.	Physical and mental retardation	.....	Optic atrophy	Bilateral Babinski signs; ataxia; increased myotatic reflexes; nystagmoid eye movements	Birth normal
28	Gowan and Masten	M	?	19 mo.	Physical and mental retardation	Grand mal epilepsy; retarded speech development	Ocular hypertelorism	Left: hemiparesis; spasticity; Babinski sign	Birth trauma
29	Goldensohn, Clardy, and Levine	F	Early infancy	11 yr.	Temper tantrums; sexual precocity	Epilepsy, grand mal and petit mal; mental retardation	Precocious sexual development	Right: divergent strabismus; supranuclear facial paresis; Babinski sign; digital tremor; dysdiadochokinesis	Birth normal; paranoid ideas
30	Derbyshire and Evans	F	6 yr.	6 yr.	Grand mal epilepsy; headache	Left hemiparesis; no development of bowel control	Ocular hypertelorism; "clubbed feet"; hemangioma of scalp	Left hemiparesis; spastic gait	Birth normal
	Pospiech								
31	Case 1	F	Birth	12 yr.	Grand mal epilepsy (8th day after birth)	Physical and mental retardation; inability to stand or walk	Coloboma right iris; choroiditis	Right facial paresis; left spastic hemiparesis; convergent paresis	Birth trauma; died at 15 yr., of lung abscess; autopsy

TABLE 2.—*Summary of Clinical Data in Cases of Agenesis of the Corpus Callosum—Continued*

Case No.	Author	Sex	Age		Symptoms		Examination		Comment
			Onset of Symptoms	Diagnosis	Initial	Subsequent	General Physical	Neurologic	
32	Case 2	F	Birth	5 yr.	Grand mal epilepsy; physical and mental retardation	Never able to walk or speak	Normal	Convergent strabismus	Birth normal; died at 6 yr., of bronchopneumonia; autopsy
33	Case 3	F	Birth	11 yr.	Physical and mental retardation	Never learned to speak	Normal	Generalized increased muscle tone; spastic gait; right Babinski sign	Birth normal
34	Palmgren and Jonsell	M	1 mo.	2.5 yr.	Feeding problem	.....	Normal	Normal	Birth asphyxia
35	Bunts and Chaffee	M	5 mo.	39 yr.	Grand mal epilepsy	Headache; confusional status; mental depression	Normal	Normal	Birth normal; megacolon
	Echternacht and Campbell								
36	Case 1	F	Birth	7 mo.	Feeding problem; physical and mental retardation	Dehydration and undernourishment	Normal	Normal	Birth normal; spina bifida occulta
37	Case 2	M	14 yr.	14 yr.	Grand mal epilepsy	Left hemiparesis; amnesia	Normal	Left hemiparesis	.....
38	Amyot	M	8 yr.	8 yr.	Grand mal epilepsy	Physical and mental retardation; inability to walk or speak	Normal	Normal	.....
39	Savitsky and Spinelli	F	Birth	6 mo.	Grand mal epilepsy	Physical and mental retardation	Hydrocephalus; optic atrophy	Increased intracranial pressure	Birth normal; autopsy
	Foster and Windholz								
40	Case 3	F	Birth	7 mo.	Grand mal epilepsy (Jacksonian)	Physical and mental retardation	Normal	Bilateral Babinski sign; transient rigidity all limbs; convergent strabismus	.....
41	Chusid, de Gutierrez-Mahoney, and Chaffee	M	?	22 yr.	Physical and mental retardation	Right hemiparesis; grand mal epilepsy	Bilateral pes cavus	Right: hemiparesis; hemihypalgesia; hemihypesthesia	.....
	Tunestam								
42	Case 1	M	4 yr.	4 yr.	Grand mal epilepsy (Jacksonian)	.....	Hydrocephalus	Bilateral Babinski sign	Birth normal
43	Case 2	F	Birth	5 mo.	Grand mal epilepsy (Jacksonian)	.....	Hydrocephalus	Normal	Birth normal
44	Svatý and Mašek	M	Birth	2 yr.	Physical and mental retardation	.....	Hydrocephalus	Left facial paresis; convergent strabismus	Birth asphyxia; autopsy
45	Sheinmel and Lawrence	M	19 yr.	24 yr.	Grand mal epilepsy	Intellectual impairment	Normal	Normal	.....

ment was reported in seven cases by Davidoff and Dyke[6] (Case 3), Köttgen,[37] Gowan and Masten,[38] Pospiech[10] (Cases 1, 2, and 3), and Amyot.[39] Two of the patients (Cases 2 and 3) reported by Pospiech were unable to speak at 5 and 11 years of age respectively. In a man aged 33 described by Mäurer,[5] speech was said to have been slow, monotonous, lacking in expression, palilalic, and sometimes explosive.

Headache was a prominent symptom in only three cases. It was the initial complaint in a case reported by Davidoff and Dyke[6] (Case 2) and preceded the onset of Jacksonian seizures by approximately two years. In a 39-year-old man (Bunts and Chaffee[33]), who had had generalized convulsions from the age of 5 months, increasingly severe headaches and more frequent seizures precipitated hospitalization. Similarly, headache was the chief complaint in a case reported by Derbyshire and Evans,[40] although convulsions antedated this symptom. No increased intracranial pressure was evident in these cases.

Dyskinesia, in the form of athetoid activity or tremor, was described in five cases. Athetoid activity was present in the upper extremities in the cases reported by Brenner[41] (Cases 3) and by Bannwarth in 1939[36] (Case 3) and 1940.[42] Noteworthy digital tremor was described by Mäurer[5] and Goldensohn, Clardy, and Levine.[32] Mäurer's patient exhibited increased muscular tone as well, suggesting a *striopallidären Störungen* of a Parkinsonian character.

The general physical status was within normal limits in 25 of these 45 cases. The following pertinent findings were mentioned in other cases: hydrocephalus, four cases (Savitsky and Spinelli[43]; Tunestam,[44] Cases 1 and 2; Svatý and Mašek[45]); optic atrophy, four cases (Bannwarth,[36] Cases 2 and 5; Kunicki and Chorobski[46]; Savitsky and Spinelli[43]); ocular hypertelorism, two cases (Gowan and Masten[38]; Derbyshire and Evans[40]); precocious sexual development and puberty, two cases (Davidoff and Dyke,[6] Case 1; Goldensohn, Clardy, and Levine[32]); macroglossia, two cases (Brenner,[41] Case 4; Bannwarth,[36] Case 4); coloboma of the optic nerve associated with pigment degeneration of the retina (Reeves,[47] Case 2); coloboma

37. Köttgen, H. U.: Die Erkennung des angeborenen Balkenmangels, Monatsschr. Kinderh. **78**:227-232 (May) 1939.

38. Gowan, L. R., and Masten, M. A.: Agenesis of the Corpus Callosum: Diagnosis of a Case by Encephalography, Am. J. Dis. Child. **60**:1381-1385 (Dec.) 1940.

39. Amyot, R.: Un cas d'agénésie du corps calleux diagnostic par la pneumoencéphalographie, Union méd. Canada **77**:667-669 (June) 1948.

40. Derbyshire, A. J., and Evans, W.: A Case of Agenesis of the Corpus Callosum: Encephalographic and Electroencephalographic Studies, Harper Hosp. Bull. **1**:17-22 (Nov.) 1941.

41. Brenner, W.: Zur Encephalographie im Kindesalter, Ztschr. Kinderh. **60**:595-622 (April) 1939.

42. Bannwarth, A.: Gehirnmissbildung und Epilepsie, Nervenarzt **13**:97-103 (March) 1940.

43. Savitsky, E., and Spinelli, V. A.: Agenesis of Corpus Callosum in Infancy: Clinical and Roentgenologic Aspects, Am. J. Dis. Child. **76**:109-115 (July) 1948.

44. Tunestam, N.: Agenesi av corpus callosum: två fall hos barn, Nord. med. **44**:1287-1288 (Aug.) 1950.

45. Svatý, J., and Mašek, R.: Agenesia of Corpus Callosum and Septum Pellucidum with Porencephaly of Cerebellum, Časop. lék. česk. **89**:1171-1177 (Oct. 20) 1950.

46. Kunicki, A., and Chorobski, J.: Ventriculographic Diagnosis of Agenesis of the Corpus Callosum, Arch. Neurol. & Psychiat. **43**:139-145 (Jan.) 1940.

47. Reeves, D. L.: Congenital Defects of the Cranial Nerves: An Associated Porencephaly and Agenesis of the Corpus Callosum Diagnosed by Ventriculography, Bull. Los Angeles Neurol. Soc. **4**:184-193 (Dec.) 1939.

of the iris associated with choroiditis (Pospiech, Case 1); microcephaly (Bannwarth,[36] Case 4), and bilateral pes cavus (Chusid, de Gutierrez-Mahoney, and Chaffee [48]). Other findings are recorded in Table 2.

The neurologic findings were within normal limits in only 14 cases. Hemiparesis, with its associated neurologic signs and sequelae, was noted in 10 cases (Davidoff and Dyke,[6] Case 1; Bannwarth,[36] Cases 1 and 2; Gowan and Masten [38]; Goldensohn, Clardy, and Levine [32]; Derbyshire and Evans [40]; Pospiech,[10] Cases 1 and 3; Echternacht and Campbell,[34] Case 2, and Chusid, de Gutierrez-Mahoney, and Chaffee [48]). Clinical evidence of diffuse neurologic lesions and/or immaturity of the neuraxis, as manifested by the bilateral Babinski sign, dyskinesia, alterations of muscular tone, impairment of coordination, and/or visual field defects, were found in 11 other cases (Davidoff and Dyke,[6] Case 2; Reeves,[47] Case 2; Brenner,[41] Case 3; Bannwarth,[36] Cases 3 and 4; Mäurer [8]; Bannwarth [42]; Kunicki and Chorobski [46]; Foster and Windholz [49]; Tunestam,[44] Case 1, and Svatý and Mašek [45]). Amyotonia was described in one case by Brenner (Case 5), and slight hemiatrophy of the right extremities was described by Hyndman and Penfield (Case 3). Convergent and divergent strabismus were relatively common, being recorded in seven cases. Increased intracranial pressure was found in two cases by Reeves (Case 2) and by Savitsky and Spinelli. Laboratory examinations of the cerebrospinal fluid gave normal results in 23 cases. Palmgren and Jonsell's [50] case was the only one in which abnormalities of the spinal fluid were found.

Pneumoencephalographic Studies.—The cardinal features of the encephalogram in agenesis of the corpus callosum enumerated by Davidoff and Dyke are widely cited and are considered pathognomonic. They are (1) marked separation of the lateral ventricles, (2) angular dorsal margins of the lateral ventricles, (3) concave mesial borders of the lateral ventricles, (4) dilatation of the caudal portions of the lateral ventricles, (5) elongation of the intraventricular foramina, (6) dorsal extension and dilatation of the third ventricle, and (7) radial arrangement of the mesial cerebral sulci around the roof of the third ventricle and extension through the zone usually occupied by the corpus callosum. Hyndman and Penfield considered the bicornuate appearance of the bodies of the lateral ventricles, symmetrical separation of the lateral ventricles, and dilatation and dorsal displacement of the third ventricle the most striking encephalographic findings. The principal encephalographic findings in these 45 cases are summarized in the following tabulation.

Findings	No. of Cases
1. Wide separation of lateral ventricles	35
2. Angular dorsal margins of lateral ventricles (bat-wing appearance)	23
3. Concave mesial borders of lateral ventricles	15
4. Dilatation of posterior horns of lateral ventricles	26
5. Elongation of intraventricular foramina	8
6. Dorsal extension and dilatation of third ventricle	36
7. Radial arrangement of sulci on medial surface of hemisphere	6
8. Dilatation of cerebral subarachnoid spaces, diffuse (cortical atrophy)	6
9. Asymmetrical dilatation of lateral ventricles	8
10. Dilatation of temporal horns of lateral ventricles	2
11. Hydrocephalus	4
12. Single, unpaired lateral ventricle (except for temporal and occipital horns)	6

48. Chusid, J. G.; de Gutierrez-Mahoney, C. G., and Chaffee, J. S.: Agenesis of the Corpus Callosum: An Electroencephalographic Study, Arch. Neurol. & Psychiat. **62**:840-846 (Dec.) 1949.

Not all the diagnostic criteria of Davidoff and Dyke were found in each case. The five commonest encephalographic features, in order of their frequency, were (1) dorsal extension and dilatation of the third ventricle, (2) marked separation of the lateral ventricle, (3) dilatation of the posterior horns of the lateral ventricles, (4) angular dorsal margins of the lateral ventricles, and (5) concave mesial borders of the lateral ventricles. It was upon these findings that the diagnosis was established in most cases. While elongation of the intraventricular foramina and radial arrangement of the sulci on the medial aspect of the hemisphere are highly characteristic of this anomaly, they evidently are not frequently encountered in encephalograms. These findings would seem to require an encephalogram of unusual technical excellence, as well as experienced interpretation.

The question whether complete or partial agenesis of the corpus callosum can be distinguished by encephalographic methods appears to be unanswered for most authors; this may account for the fact that only 7 of these 45 cases were thought to represent partial agenesis of the corpus callosum. Gowan and Masten considered their case to be one of partial agenesis because no elongation of the intraventricular foramina was observed. If this reason were a valid one, most of the reported cases would be relegated to this category. Hyndman and Penfield had three cases in which the diagnosis was partial agenesis of the corpus callosum, and in each instance the third ventricle was dilated and elevated in a peculiar manner. In Cases 3 and 5 the caudal portions of the third ventricle seemed to curve upward above the level of the lateral ventricles (as seen in the lateral projections). They concluded that this finding indicated an agenesis of the posterior corpus and/or splenium of the corpus callosum, no dorsal extension of the rostral portion of the third ventricle being possible because of the genu and rudimentary anterior corpus. Pospiech,[10] the only author who reported antemortem diagnoses of both complete and partial ageneses of the corpus callosum later confirmed by autopsy, supported the conclusions of Hyndman and Penfield. Items 8 through 11 in the tabulation do not appear to have any special diagnostic significance in agenesis of the corpus callosum, but were associated findings.

Bannwarth [51] reported a total of six cases of *Gehirnmissbildungen* diagnosed by encephalographic methods in which the lateral ventricles were unpaired except for the occipital and temporal horns. The third ventricle was usually moderately dilated, and no evidence of hemispheric separation was found. He interpreted the results of these studies as indicating complete agenesis of the fornix, septum pellucidum, hippocampal commissure, and corpus callosum and supported his thesis by pathologic material reported by Goldstein and Riese,[52] Hinrichs,[53] and Beck.[54] Bannwarth's

49. Foster, S. E., and Windholz, F.: Radiological Studies in Rare But Typical Cerebral Malformations: Encephalographic Findings in Cerebral Hemiagenesis; Absence of the Corpus Callosum and Absence of Septum Pellucidum, Stanford M. Bull. **6**:395-406 (Aug.) 1948.

50. Palmgren, A., and Jonsell, S.: Agenesie des Corpus callosum durch Encephalographie diagnostiziert, Ztschr. Kinderh. **63**:318-327 (Sept.) 1942.

51. Bannwarth, footnotes 36 and 42.

52. Goldstein, K., and Riese, W.: Klinische und anatomische Beobachtungen an einem vierjährigen riechhirnlosen Kinde, J. Psychol. u. Neurol. **32**:291-311, 1926.

53. Hinrichs, U.: Über eine durch Balken- und Fornixmangel ausgezeichnete Gehirnmissbildung, Arch. Psychiat. **89**:57-101, 1930.

54. No reference was cited and none could be found in the literature.

cases appear unique and probably represent a very different type of developmental defect, occurring at a much earlier time. According to the classification postulated by Bruce, arrested development of this type probably occurred prior to the third week of fetal life.

Porencephalic cysts, in addition to agenesis of the corpus callosum, were reported in six cases by Reeves [47] (Case 2); Bannwarth [36] (Case 3); Bunts and Chaffee [33]; Foster and Windholz [49]; Chusid, de Gutierrez-Mahoney, and Chaffee,[48] and Svatý and Mašek.[45] Foerster's [55] case was most unusual; a diverticulum, thought to be derived from the paraphysis, occurred in association with complete agenesis of the corpus callosum. The paraphysial diverticulum was removed surgically and identified histologically. Removal was followed by complete freedom from the Jacksonian seizures.

Pathologic confirmation of encephalographic data has been meager to date in that in only seven cases has the diagnosis been verified by necropsy (Table 1). Surgical exploration was undertaken in seven cases, but in only five was the diagnosis confirmed by this means. In the two cases in which surgery failed to elucidate the anomaly the diagnosis was later confirmed by autopsy (Davidoff and Dyke, Case 1) and by comparison with a subsequent case (Hyndman and Penfield).

Other Roentgenologic Studies.—A plain roentgenogram of the skull was apparently not helpful in making the diagnosis of agenesis of the corpus callosum, for detailed reports of this examination were infrequent and such data as were offered were noncontributory.

Cerebral angiograms have been obtained in at least two cases of agenesis of the corpus callosum. Mäurer [8] employed this method in his case in which a previous diagnosis had been made by encephalographic means. He observed an increase in the caliber of the right anterior cerebral and pericallosal arteries, with minimal, if any, deformity. Tarlov and Rosenberg [56] obtained a cerebral arteriogram on a 17-month-old infant with arrested hydrocephalus who died after the procedure. Autopsy revealed agenesis of the corpus callosum, but the arteriogram did not suggest this abnormality.

Electroencephalography.—It is somewhat surprising to find that electroencephalographic studies were done in only four cases (Derbyshire and Evans, Goldensohn, Clardy, and Levine; Bunts and Chaffee, and Chusid, de Gutierrez-Mahoney, and Chaffee) in this series, in which convulsive disorders featured so prominently. Although the electroencephalographic records were periodically "within normal limits," they disclosed bursts of high-amplitude, slow activity and were characteristic of convulsive disorders. In the first three cases above cited a lack of "synchronization" of activity was noticeable in the occipital region. In at least two of these four cases agenesis of the corpus callosum was associated with porencephaly (Bunts and Chaffee, Chusid, de Gutierrez-Mahoney and Chaffee), rendering interpretations of the role of the corpus callosum difficult.

55. Foerster, O.: Ein Fall von Agenesie des Corpus callosum verbunden mit einem Diverticulum paraphysarium des Ventriculus tertius, Ztschr. ges. Neurol. u. Psychiat. **164**:380-391, 1939.

56. Tarlov, I. M., and Rosenberg, M.: Cerebral Angiography with Iodopyracet Injection U. S. P. (Diodrast®): Its Dangers Particularly in Hydrocephalic Patients, A. M. A. Arch. Neurol. & Psychiat. **67**:496-509 (April) 1952.

Miscellaneous Cases: The literature disclosed several cases in which descriptions and illustrations of the encephalograms were strikingly similar to those found in agenesis of the corpus callosum, but which carried other diagnoses. Fränkel and Koschewnikow [57] published a case (Case 10) in which the encephalogram revealed marked separation of the lateral ventricles and dilatation and dorsal extension of the third ventricle; a diagnosis of oligophrenia was made. In a case (C. G.) reported by the staff of the Royal Aberdeen Hospital for Sick Children,[58] the encephalogram demonstrated (1) wide separation of the lateral ventricles, (2) dilatation and upward extension of the third ventricle, (3) angular dorsal margins of the lateral ventricles, (4) elongation of the intraventricular foramina, and (5) striking dilatation of the occipital horns of the lateral ventricles. The authors remarked upon the "bizarre" appearance of the encephalogram but "could offer no explanation of it." The final diagnosis was congenital amentia. In Laubenthal's [59] Case 3, in which the diagnosis was communicating cyst of the cavum septi pellucidi, an 18-year-old youth had onset of grand mal seizures at the age of 10 years. Plain roentgenograms of the skull disclosed a midline calcification 3 fingerbreadths above the sella turcica, and encephalograms revealed (1) widely separated lateral ventricles, (2) dilatation of the third ventricle with dorsal extension above the level of the lateral ventricles, and (3) angular dorsal margins of the lateral ventricles. Roentgenograms of the skull one year later showed no change in the appearance of the calcification. It is likely that agenesis of the corpus callosum probably existed to some degree in each case.

List, Holt, and Everett [60] reviewed the literature of lipomas of the corpus callosum, mainly clinicopathologic material, and found 10 cases in which lipoma was associated with partial agenesis, hypoplasia, or atrophy of the corpus callosum. In one case (Huddleson [61]) a lipoma was found in the usual position of the corpus callosum, the latter structure being completely absent. It has been postulated that agenesis of the corpus callosum is secondary to the lipoma formation, the lipoma inhibiting the formation and development of the corpus callosum.

REPORT OF CASES

Reports of two cases of agenesis of the corpus callosum diagnosed during life follow.

CASE 1.—J. J. T., a man aged 24, was admitted to United States Naval Hospital, St. Albans, N. Y., on March 21, 1950, several hours after having had his first generalized convulsion. On the night prior to admission the patient consumed a moderate amount of alcohol, but was said not to have been intoxicated. No recognizable aura preceded the seizure. The patient gave a sudden, panicky shriek, fell to the ground, turned his head to the right, and began to salivate

57. Fränkel, S. R., and Koschewnikow, A. M.: Die Encephalographie bei Psychischen- und Nervenkrankheiten des Kindes- und Säuglingsalters, Acta radiol. **14**:349-374, 1933.

58. Staff of the Royal Aberdeen Hospital for Sick Children: Encephalography in the Investigation of Certain Cerebral Conditions in Childhood, Arch. Dis. Childhood **11**:97-126 (June) 1936.

59. Laubenthal, F.: Über Veränderungen des Septum pellucidum, Nervenarzt **10**:401-411, 1937.

60. List, C. F.; Holt, J. F., and Everett, M.: Lipoma of the Corpus Callosum: Clinico-Pathologic Study, Am. J. Roentgenol. **55**:125-134 (Feb.) 1946.

61. Huddleson, J. H.: Ein Fall von Balkenmangel mit Lipomentwicklung in Defekt, Ztschr. ges. Neurol. u. Psychiat. **113**:177-192, 1928.

profusely; tonic and clonic movements soon appeared in all extremities. No tongue biting or loss of bowel or bladder control was noted. The duration of the seizure was estimated to have been about three minutes. After the attack the patient was confused, lethargic, and somewhat amnesic.

The birth history was not obtainable, but the family history was not remarkable, and the system review showed nothing abnormal. No significant cranial trauma was known to the patient.

General physical and neurologic examinations were entirely within normal limits. Lumbar puncture revealed a crystal-clear cerebrospinal fluid under normal tension; results of routine laboratory studies of the spinal fluid were normal. Plain roentgenograms of the skull were not remarkable. A pneumoencephalogram taken on May 4, 1950, revealed widely separated lateral ventricles with a bicornuate appearance and a dilated third ventricle, with definite dorsal extension. The mesial borders of the lateral ventricles were concave, and the dorsal margins of the lateral ventricles appeared angular. In the posteroanterior and lateral projections the posterior horns of the lateral ventricles appeared moderately dilated. The electroencephalographic report was as follows: "The record is moderately abnormal, revealing scattered fast and slow frequencies throughout, without focal or lateralizing significance. The record is consistent with

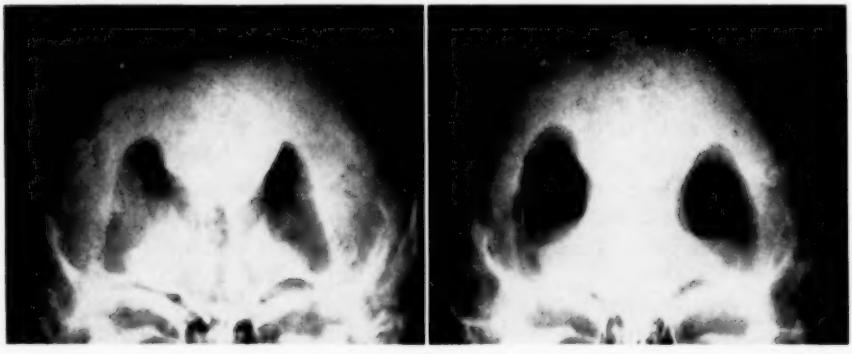

Fig. 1 (Case 1).—Anteroposterior projection (left) of encephalogram, showing widely separated lateral ventricles, concave mesial borders of lateral ventricles, angular dorsal margins of lateral ventricles, and dilatation and dorsal displacement of the third ventricle. Posteroanterior projection (right) of encephalogram, demonstrating widely separated lateral ventricles and dilatation of the posterior horns.

a deep, centrally placed lesion." The surgeon in charge of the case interpreted the findings as indicating a tumor of the corpus callosum, possibly a lipoma. On July 21, 1950, a right frontal craniotomy was performed, and exploration of the area in question was said to have revealed nothing significant. The corpus callosum was said to have been identified, and no tumor was found. The consultant neurosurgeon who assisted with the operation, when questioned later concerning the operative findings, stated that no corpus callosum was found. After operation the patient exhibited moderate left hemiparesis, nystagmus on extreme lateral gaze to both the right and the left, and limitation of upward gaze. Within a relatively short time these neurologic deficits cleared, except for minimal weakness of the left extremities. On Feb. 28, 1951, the patient was discharged from active naval service, with the impression that he had an inoperable brain tumor. Although anticonvulsant therapy controlled the seizures completely, the patient was a psychic "cripple," unable to work or pursue any useful activity because of his anxiety. He first came to my attention in October, 1951, when he was readmitted at his own request for reevaluation. The findings in general physical and neurologic examination were unremarkable except for minimal residual weakness in the left extremities. Plain roentgenograms of the skull disclosed the right cranial defect resulting from the previous craniotomy and multiple Cushing clips deep within the substance of the brain, but otherwise showed an essentially normal condition. Another pneumoencephalogram was performed, with the same findings as those previously

noted. The electroencephalogram revealed roughly symmetrical activity of predominantly 5 to 6 cps waves with frequent spiking and the maximal amount of slow activity in the right parietal leads. The amplitude of the waves was greater over the right hemisphere. A diagnosis of partial agenesis of the corpus callosum was made. Upon discharge from the hospital the patient was greatly relieved, knowing that he did not have "brain tumor."

CASE 2.—L. V. P., a man aged 20, was first admitted to the United States Naval Hospital, St. Albans, on Dec. 26, 1950, because of a generalized convulsion which had occurred the

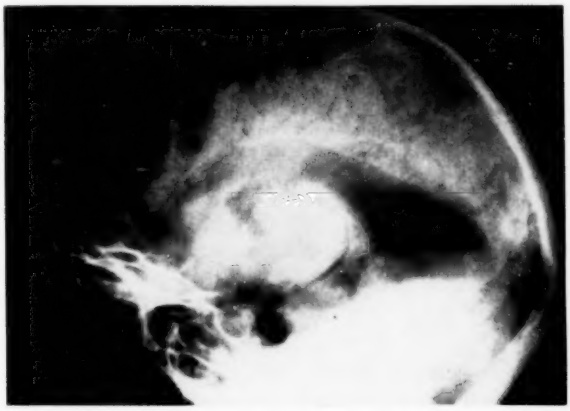

Fig. 2 (Case 1).—Lateral projection of encephalogram, showing moderate dilatation of the posterior horns of the lateral ventricles.

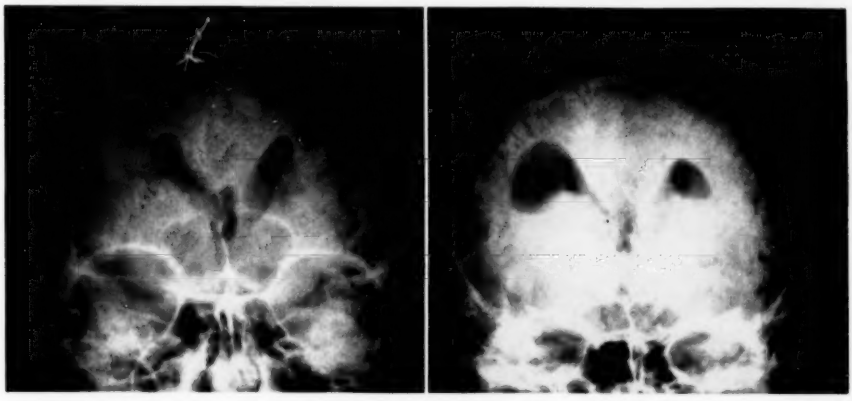

Fig. 3 (Case 2).—Anteroposterior projection (left) of encephalogram demonstrating wide separation of the lateral ventricles and their bicornuate appearance. The third ventricle is dilated and displaced upward. Posteroanterior projection (right) encephalogram, showing dorsal extension of the third ventricle, as well as wide separation of the lateral ventricles and angular dorsal margins.

previous night. On Christmas Day he had indulged in excessive eating and drinking, without apparent ill effects. Shortly after going to bed, he had a generalized seizure, without aura or focal features. On admission the patient was alert and cooperative and responded to all questions in an intelligent manner. The findings on general physical and neurologic examination

were normal, as were the results of routine laboratory studies and examination of the spinal fluid. Plain roentgenograms of the skull disclosed a fine curvilinear calcification to the right of the midline in the anteroposterior projection, but otherwise nothing abnormal. A pneumoencephalogram done on Jan. 16, 1951, was reported to have revealed "moderate separation of the anterior horns of the lateral ventricles and an area of decreased density in the vicinity of the corpus callosum." The electroencephalogram showed occasional runs of 5- to 6-cps waves of moderate voltage, without any definite focal pattern. This record was considered moderately abnormal and consistent with a convulsive disorder. The neurosurgeon in charge of the case believed that the findings were consistent with a lipoma of the corpus callosum. However, since the seizures were easily controlled by anticonvulsant drugs and localizing neurologic signs were lacking, surgical intervention was not advised. A second electroencephalogram, done on March 15, disclosed low-voltage fast activity; the slow activity previously present was not seen. This record was considered a normal interseizure one. The patient was discharged from active duty on April 20, 1951.

After discharge the patient continued anticonvulsant therapy only two weeks. Upon discontinuation of the drugs two generalized convulsions occurred, both during sleep. Thereafter no further seizures occurred until March 4, 1952. During this period the patient was employed satisfactorily as a bank teller and established a good work record. Aside from occasional generalized headache, described as "throbbing" in character, the patient had no complaints.

This patient was first seen by us on March 5, 1952, having sought admission because of the seizure on the day before. The general physical status was normal; neurologic examination disclosed minimal right epipraxic tremor in the finger-to-nose test and generally sluggish myotatic reflexes. X-ray examination of the skull showed no change in the small curvilinear calcification to the right of the midline. Electroencephalographic records demonstrated 2- to 3-cps, high-amplitude activity on hyperventilation, with delay in return to the basic pattern. On March 13, an encephalogram, technically superior to the one obtained a year earlier, disclosed widely separated lateral ventricles, with a bicornuate appearance, and an enormously dilated third ventricle, extending dorsally almost to the upper border of the lateral ventricles. The dorsal margins of the lateral ventricles appeared angular, and the mesial border of the right lateral ventricle was concave. No dilatation of the posterior horns of the lateral ventricles was noticeable. A right cerebral arteriogram, done on March 17, appeared to be within normal limits.

COMMENT

It is apparent from this material that the diagnosis of agenesis of the corpus callosum during life is practically impossible to make on the basis of clinical findings, but can readily be made by encephalography. The encephalographic findings are distinctive and pathognomonic of the condition, though the differential diagnosis would seem to require at least basic knowledge of neuroanatomy and gross neuropathology. The conditions with which agenesis of the corpus callosum may be confused are communicating cyst of the cavum septi pellucidi and lipoma of the corpus callosum. The encephalogram in cases of communicating cyst of the cavum septi pellucidi usually does not present the bicornuate appearance of the lateral ventricles in the anteroposterior projection, the angular dorsal margins of the lateral ventricles, the elongation of the intraventricular foramina, or the radial arrangement of the sulci on the medial aspects of the hemispheres. The cyst may be confused with a dilated third ventricle, but dorsal extension of the cyst is limited by the corpus callosum. In cases of lipoma of the corpus callosum the differential diagnosis by encephalography may be more difficult, since in approximately one-third of the cases partial agenesis, hypoplasia, or atrophy of the corpus callosum may coexist, according to List, Holt, and Everett.[60] These authors have reported that a plain roentgenogram of the skull frequently is helpful if it reveals an area of radiolucency in the

region of the corpus callosum and/or calcification. In cases of lipoma of the corpus callosum not associated with agenesis the tumor would seem to prevent dorsal extension of the third ventricle.

One of the interesting clinical features of this condition is the relatively tardy onset of convulsive disorders in certain cases. In nine of the cases collected from the literature and in the two current cases convulsive disorders began in the second and third decades of life. Explanation of this phenomenon is extremely difficult. The two currently reported cases are unusual in that both patients were in good health and without complaints until the onset of their convulsive disorder, early in the third decade of life.

It would seem evident from this review of the literature, and from the resulting professional differences of opinion at the operating table, as mentioned in the report of our first case, that recognition of complete or partial agenesis of the corpus callosum at operation may sometimes prove difficult, even for surgeons of considerable experience. In contrast, the diagnosis of agenesis of the corpus callosum can be made with comparative ease by encephalographic methods. Simple agenesis of the corpus callosum should not offer serious difficulties in differentiation from neoplasms of that region, since evidence of an expanding intracranial lesion is generally lacking. Surgical intervention, having been demonstrated to be a poor diagnostic aid in cases of agenesis of the corpus callosum, as well as possessing no therapeutic value, would seem contraindicated unless unequivocal signs of an expanding intracranial lesion coexist.

SUMMARY AND CONCLUSIONS

A review of the literature on agenesis of the corpus callosum disclosed 43 cases in which the diagnosis was made during life by encephalography. Encephalograms were made in at least two other cases, but the diagnosis was not made until necropsy. We report two additional cases in which the diagnosis was made during life. Analysis of this material revealed the following facts:

1. In institutions in which a great number of encephalographic studies were performed, the highest incidence of agenesis of the corpus callosum diagnosed during life was 3%.

2. Initial symptoms manifested in cases of agenesis of the corpus callosum became apparent prior to 2 years of age in 53% and prior to 10 years of age in 17%. Only in the two cases currently reported did the initial symptoms appear after the age of 20.

3. Grand mal epilepsy was the initial symptom in 42% of the cases, while physical and/or mental retardation was the first symptom noted in 42%.

4. Nearly 60% of the patients in this series had grand mal seizures sometime during the course of their illness; such seizures were said to have been, or were described as, Jacksonian in type in 42% of the cases. Petit mal epilepsy was described in only four cases.

5. Physical and neurological findings varied greatly and did not appear to present any characteristic features. Hemiparesis and/or diffuse pathologic changes within the neuraxis were clinically demonstrable in about 45% of the cases. This material would not seem to support the thesis of a specific syndrome of the corpus callosum.

6. The encephalographic criteria used in making the diagnosis were those established by Davidoff and Dyke. The five commonest encephalographic findings, in order of their frequency, were as follows: (*a*) dorsal extension and dilatation of the third ventricle; (*b*) wide separation of the lateral ventricles; (*c*) dilatation of the posterior horns of the lateral ventricles; (*d*) angular dorsal margins of the lateral ventricles, and (*e*) concave mesial borders of the lateral ventricles.

As far as can be determined from the literature, the diagnosis of agenesis of the corpus callosum during life has been made only by encephalographic studies. The usefulness of cerebral arteriography in the diagnosis of this anomaly remains to be established.

TEST OF "THE ABSTRACT ATTITUDE" IN CHIMPANZEES FOLLOWING ABLATION OF PREFRONTAL CORTEX

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AND
H. W. NISSEN, Ph.D.
ORANGE PARK, FLA.

LASHLEY [1] demonstrated that the deficit in learning and retention following cortical ablations in rats is a function of the amount of tissue removed, rather than of the locus of such removals. The search for regional specialization of function in the cortex of higher mammals, however, has continued, encouraged, no doubt, by the notion of increasing corticalization in evolutionary development. To the prefrontal areas of the cortex are usually assigned the function of mediating higher mental processes, characteristic of the primates, and especially of man. These processes are usually hazily specified, with vague references to inferential thinking, symbolism, mental synthesis, and the like.

There have been various attempts, however, to define the function of the frontal lobes more exactly, usually by assigning to them some basic process which enters into a variety of intelligent performances. Thus, Jacobsen [2] suggested that they are essential for the "immediate memory" which underlies solution of the delayed reaction, the multiple-platform stick-using task, and similar problems. Malmo [3] proposed that they provide the capacity to resist "retroactive inhibition." Settlage, Zable, and Harlow [4] came to the conclusion that these areas serve to counteract "perseverative interference," and Lashley [5] suggested that they help to overcome the "confusion of situations which have much in common but require different reactions." Gelb and Goldstein,[6] Weigl,[7] and Goldstein [8] proposed that the frontal

From Yale University and the Yerkes Laboratories of Primate Biology, Inc.

1. Lashley, K. S.: Brain Mechanisms and Intelligence: A Quantitative Study of Injuries to the Brain, Chicago, University of Chicago Press, 1929.

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7. Weigl, E.: Zur Psychologie sogenannter Abstraktionsprozesse, Ztschr. Psychol. **103**:2-45, 1927; J. Abnorm. & Social Psychol. **36**:3-33, 1941.

8. Goldstein, K.: Aftereffects of Brain Injuries in War: Their Evaluation and Treatment, New York, Grune & Stratton, Inc., 1942.

lobes subserve the "abstract attitude" and that when these are destroyed the patient is left with only the more primitive "concrete attitude." These writers and others (Vigotsky,[9] Bolles,[10] and Goldstein and Scheerer[11]) found a deficiency of the abstract attitude also in the feebleminded, in schizophrenic persons, and in patients with lesions of other cortical regions. Goldstein[8] stated that, although the abstract attitude may be impaired by any brain injury, the deficiency is most pronounced after lesions of the frontal lobes. King,[12] however, reported no loss of abstraction in human patients with selective partial ablations of the prefrontal regions.

Of the various kinds of tests for impairment of the abstract attitude, the most used and useful, apparently, is the sorting test. The patient is given a number of objects which differ among themselves but which also have some characteristics in common. He is told to sort them into groups of objects which "belong together." Having made one classification, say in terms of the several colors represented, the patient is told to resort them in some other way. The aspects permitting categorization are usually those of color, form, size, use or function, and material composition.

Impairment of the abstract attitude is indicated when the patient fails to make any groupings at all, except perhaps of pairs of objects identical in all respects. He may protest, correctly, that the several red objects are different—in respect to form, size, or material—and will resist the suggestion that nonidentical red objects do belong together. Or, having made a classification on the basis of one aspect, the patient may be unable to shift to other possible bases of categorization.

Weigl[7] defined the "feat of abstraction" as consisting in "either voluntarily or involuntarily singling out, i. e., 'abstracting the common partial content' from all the *de facto* given contents." Goldstein[8] listed six rather nebulously defined "potentialities," such as "detaching the ego from the outer world" and "assuming a mental set voluntarily," as based on the abstract attitude. The inability to shift from one aspect to another is termed "rigidity." Bolles[10] suggested that "the basis of pertinence" for classification may be any one of four types: identity ("The subject brings together only those objects which are exact sensory equivalents"); partial identity ("The subject brings objects together that are similar . . . equivalent in terms of some one sensory attribute"); cofunctionality ("the objects seem to belong together in a concrete situation, . . . being used together in a specific set of circumstances"), and categorical similarity ("The objects are taken as representative of a class and not in terms of some specific attribute or function"). Bolles considered these types as "regions in a continuum extending from the extremely concrete to the most abstract types of behavior."

9. Vigotsky, L. S.: Thought in Schizophrenia, Arch. Neurol. & Psychiat. **31**:1063-1077, 1934.

10. Bolles, M. M.: The Basis of Pertinence: A Study of the Test Performance of Aments, Dements and Normal Children of the Same Mental Age, Arch. Psychol., No. 212, 1937, pp. 1-51.

11. Goldstein, K., and Scheerer, M.: Abstract and Concrete Behavior: An Experimental Study with Special Tests, Psychol. Monogr. **53**:1-151, 1941.

12. King, W. R.: Ability to Abstract, in Mettler, F. A., Editor: Selective Partial Ablation of the Frontal Cortex: A Correlative Study of Its Effects on Human Psychotic Subjects, New York, Paul B. Hoeber, Inc., 1949.

The central principle of the sorting test is incorporated in the matching and oddity tests as used with monkeys [13] and apes.[14] In place of verbal instruction, the animal is trained in the matching test to choose the object (or objects) which matches a sample object. If it chooses the object which is like the sample, it is rewarded; if it chooses a dissimilar object, it is not rewarded. (In the oddity test the requirements are reversed; the one object which is different from the other two, or more similar, objects must be chosen.) By presentation of objects differing in only one aspect, e. g., color, on any given trial, the ability of the animal to utilize various "bases of pertinence" can be tested. In conditional matching, neither choice object is exactly like the sample; one object matches the sample in respect to color, the other one in respect to form. The animal's task is then to choose the form- or color-matching object in accordance with a conditional cue, such as brightness of the background. Conditional matching thus requires rapid, trial-to-trial shifts from one sensory basis of categorization to another, involving what Harlow [13a] has called "the Weigl principle." Weinstein [15] carried this categorizing performance to the point where two achromatic samples, whose differing forms had previously been associated with red and blue respectively, determined the choice of either red or blue choice objects. This performance belongs in the region of Bolles' fourth type of pertinence.

PRESENT INVESTIGATION

The present experiment employed a testing procedure which emphasizes certain critical features of the sorting test. It is a modification of a technique previously employed with chimpanzees.[16] The animals were first overtrained on a multiple-cue visual discrimination problem. The positive and negative choice objects differed in respect to size, form, and color (specifically, a large black square versus a small white triangle). In a subsequent series of tests, pairs of objects were presented the members of which differed from each other in only one of these dimensions (e. g., a large black square versus a small black square). In a third step of the procedure, the subjects had to learn the reverse of the original habit.

The initial problem could be solved by responsiveness to any one of three available cues: size, form, or color. The single-cue tests would indicate the scope of the animal's responsiveness and its ability to "abstract" the component aspects of the original, "concrete" stimulus pattern. Chance performance on all single-cue tests would indicate a severe loss of the "abstract attitude"—a failure to respond to the sensory similarity between the training and the test objects, and a dependence on the complete, unaltered stimulus patterns used in training. Since single-cue tests

13. (*a*) Harlow, H. F.: Solution by Rhesus Monkeys of a Problem Involving the Weigl Principle Using the Matching-from-Sample Methods, J. Comp. Psychol. **36**:217-227, 1943. (*b*) Young, M. L., and Harlow, H. F.: Generalization by Rhesus Monkeys of a Problem Involving the Weigl Principle Using the Oddity Method, ibid. **36**:201-216, 1943.

14. Nissen, H. W.; Blum, J. S., and Blum, R. A.: Analysis of Matching Behavior in Chimpanzee, J. Comp. & Physiol. Psychol. **41**:62-74, 1948; Conditional Matching Behavior in Chimpanzee: Implications for the Comparative Study of Intelligence, ibid. **42**:339-356, 1949.

15. Weinstein, B.: Evolution of Intelligent Behavior in Rhesus Monkeys, Genet. Psychol. Monogr. **31**:3-48, 1945.

16. Nissen, H. W., and Jenkins, W. O.: Reduction and Rivalry of Cues in Discrimination Behavior of Chimpanzees, J. Comp. Psychol. **35**:85-95, 1943.

of size, form, or color were presented within the same session, rapid shifts of responsiveness from one aspect to another were involved. The "partial identities" to which the animal could respond, however, were between present sensory input and the after-effects of previous sensory experiences, rather than among an array of immediate perceptions, as in the sorting test. Relative difficulty of learning the reversed habit provides a further index of "rigidity." The data of this study show no significant differences in any of the described measures between two animals with ablations of the prefrontal cortex and two normal (control) subjects.

In addition to intellectual deficits, prefrontal ablation is said to produce emotional-attitudinal changes. Lobotomy or ablation in this region is reported to produce a lowering of anxiety and tension in man [17] and a decrease of emotional response to frustration in chimpanzees.[18] Contrary to expectation, the experimental subjects of this study were more emotionally responsive to frustration than were the controls.

Subjects.—Four male chimpanzees were used: Alan, aged 47 months; Ked, 48 months; Verb, 63 months, and Dehn, 67 months, at the time of experimentation. The two normal (N) animals, Verb and Dehn, previously had limited experience in formal discrimination learning. The two experimental animals had no prior experience in formal training. At the age of 2 months, Alan (Op) had a one-stage bilateral prefrontal lobectomy. In general development and cage behavior, Alan has shown no deviations falling outside the normal range. He is a bit aggressive and is rather large. Ked (Op) likewise had a bilateral ablation of the prefrontal cortex performed in one stage at the age of 2 months. In these operations the attempt was made to remove all frontal lobe tissue anterior to Area 8. One month later, Ked had a partial removal of the posterior parietal cortex. Ked (Op) is a friendly, rather mild-mannered, but self-reliant subject. He is smaller than average, but the weights of all four subjects are within the normal range. He adopted a sitting posture which we have previously seen only in an animal (Rob) whose upper and lower extremities were from an early age encased in cardboard cylinders; this posture is fully described elsewhere.[19] It is possible that Ked's unusual sitting posture is a function of damage produced by the parietal lesion. In other respects, Ked's development and behavior fall within the normal range.

All cortical ablations were performed by Dr. Karl H. Pribram. Further operative details and a description of the lesions will be given after tests of other intellectual functions have been completed and the brains have become available for study.

Apparatus and Procedure.—The stimulus objects were cut from ¼ in. (6 mm.) plywood. In the initial problem (Step 1, below) the positive object was a 6 by 6 in. (15 by 15 cm.) square, painted black; the negative object was an isosceles triangle of 4¾ in. (12 cm.) base and altitude, painted white. The objects were presented in the vertical plane, 7½ in. (19 cm.) from center to center. The subject, pushing with his fingers against either object, uncovered a food well which was baited or empty. The stimulus objects were presented in our standard discrimination apparatus, which was wheeled up to the 2 in. (5 cm.) mesh-wire partition of the animals' living cage. For baiting and placement of the objects, the platform containing the food wells was drawn back, behind an opaque screen, and for response it was pushed forward against the cage partition.

Fifty or 53 trials were given per session, with one or two sessions per day. A systematically randomized left-right sequence was used, the correct object being on the same side not more

17. Freeman, W., and Watts, J. W.: Psychosurgery: Intelligence, Emotion and Social Behavior Following Prefrontal Lobotomy for Mental Disorders, Springfield, Ill., Charles C Thomas, Publisher, 1942.

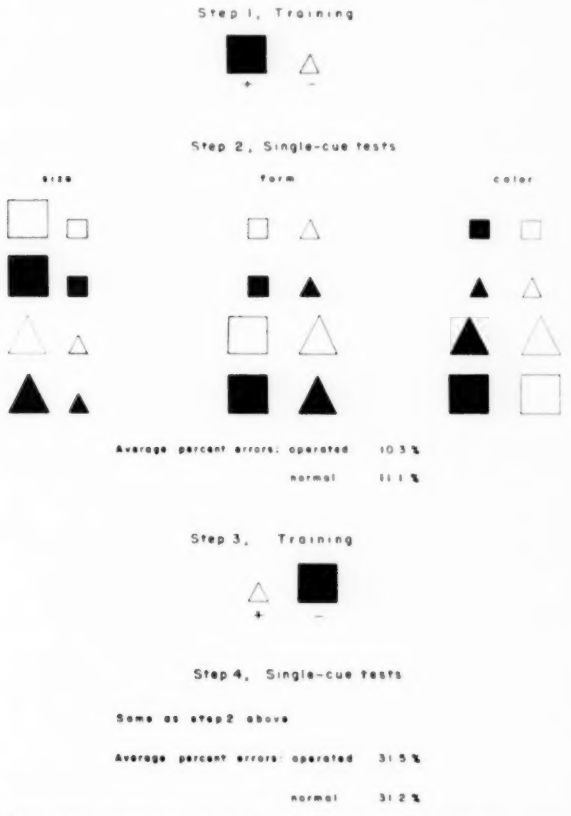
18. Jacobsen, C. F.; Wolfe, J. B., and Jackson, T. A.: An Experimental Analysis of the Functions of Frontal Association Area in Primates, J. Nerv. & Ment. Dis. **82**:1-14, 1935.

19. Nissen, H. W.; Chow, K. L., and Semmes, J.: Effects of Restricted Opportunity for Tactual, Kinesthetic, and Manipulative Experience on the Behavior of a Chimpanzee, Am. J. Psychol. **64**:485-507, 1951.

than four times in succession. The noncorrection technique was used. In both training and testing trials, only the food well under the correct object was baited. The reward on each trial consisted of a small piece of fruit, vegetable, or cracker from the animal's regular diet allotment; except for milk, most of the day's food was given as rewards in the experiment.

The sequence of training-testing procedure was the same for all subjects (Figure):

STEP 1: Training in the basic discrimination—large black square (positive) versus small white triangle (negative). Each animal was given 500 trials, of which the last 150 were, in each case, without error.



Stimulus objects used in Steps 1, 2, 3, and 4 with all subjects and summary of results.

STEP 2: Single-cue tests. Twenty sessions of 50 trials each were given. The first four trials of each session, and every fourth trial thereafter, were further training trials, as in Step 1, given in order to maintain the basic discrimination. The remaining 36 trials of each session were single-cue tests: 12 size, 12 color, and 12 form tests. (Each single cue was presented equally often in the four different contexts of the nondifferential aspects. In the size tests, for instance, the larger and smaller objects were black squares, white squares, black triangles, or white triangles. The same combination was never given in immediate succession.)

STEP 3: Training in reversal of the basic discrimination, i. e., small white triangle (positive) versus large black square (negative), to a criterion of not more than 1 error within a session of 50 trials. The number of trials per subject varied from 100 to 224 (Table).

STEP 4: Single-cue tests based on the reversed habit. Immediately after Step 3, each subject was given five sessions of 53 trials each. The 1st, 14th, 27th, 40th, and 53d trials were repetitions of the basic (reversed) habit, as in Step 3; the remaining 48 trials were single-cue tests presented according to a schedule similar to that described under Step 2 except that each of the 12 combinations was presented four times in a session. This series gave a total of 80 size tests, 80 form tests, and 80 color tests, each differential cue being presented 20 times in each of the four context conditions.

RESULTS AND COMMENT

Initial Learning and Reversal Learning.—The Table summarizes results for the two animals with brain operations and the two normal animals. Two subjects, Alan (Op) and Verb (N), had an initial preference for the positive object (Step 1); of the other two animals, the experimental one learned somewhat faster. In the reversal training (Step 3) both experimental animals learned with fewer errors than did either normal subject. These differences, however, are within the

Learning, Reversed Learning, and Test Scores for Experimental and for Control Subjects

		Experimental		Normal (Control)	
Step *		Alan	Ked	Verb	Dehn
1	Initial training, no. of errors in 500 trials....	0	22	1	53
2	Single-cue tests, 1st series, % of errors				
	Size †.....	0.4	5.8	2.5	4.6
	Form †.....	1.7	10.4	15.4	10.8
	Color †.....	17.1	26.3	25.4	7.9
	% of errors in 720 tests.....	6.4	14.2	14.4	7.8
3	Reversal training, no. of errors.....	18	47	69	120
	Reversal training, trials to criterion.....	100	150	150	224
4	Single-cue tests, 2d series, % of errors				
	Size ‡.....	8.8	15.0	8.8	16.3
	Form ‡.....	27.5	37.5	27.5	42.5
	Color ‡.....	66.3	33.8	80.0	12.5
	% of errors in 240 tests.....	34.2	28.7	38.7	23.7

* See section on procedure.
† In this series 240 tests were made on each subject.
‡ In this series 80 tests were made on each subject.

usual range of individual variability in learning rate. There is no evidence here, at any rate, that the loss of cortical tissue produced slower initial learning or less plasticity in reversing the original habit.

Single-Cue Tests.—The total number of errors in the single-cue tests (Steps 2 and 4) is very similar for the two groups (Table and Figure). The totals in Step 2 are 148 for the animals operated on and 160 for the normals; in Step 4 they are 151 and 150 respectively.

In Step 2, all the animals, both normal and experimental were able to discriminate on the basis of each of the three component properties of the training stimuli presented singly. The two lowest scores on any of these single-cue tests were those of Ked (Op) and Verb (N), who made 63 and 61 errors, respectively, on the color tests; both these scores (74 and 75% correct) are significantly above chance at the 0.001 level. In Step 4, following reversal of training, there was a general decrease in accuracy of response to the isolated cues. This may have been a function of (*a*) the lower criterion of learning (1 error in 50 trials versus no errors in 200 trials),

(*b*) the smaller number of interpolated training trials in Step 4, and (*c*) interference produced by perseverance of the effects of the training-testing conditions of Steps 1 and 2. Even in Step 4, however, there were only two cases, both tests to the color cue, in which accuracy dropped below that of chance: Alan (Op) 34% and Verb (N) 20%.

For both groups, the order of increasing percentage of errors in the single-cue tests was in those for size, form, color; individual exceptions were Dehn (N), in Steps 2 and 4, and Ked (Op), in Step 4. All four subjects showed a decrease of errors from the first to the last half of each of the testing periods Steps 2 and 4. Since the single-cue tests were differentially rewarded, this decrease probably represents, in part at least, a progressive learning of the 12 test pairs. (Except for differential rewarding, our procedure was designed to minimize learning of the test objects.) There was no consistent group difference in improvement within Steps 2 and 4. It may be noted that the scores of Alan (prefrontal lobectomy only) were better in Steps 2 and 3 than were those of Ked (prefrontal and parietal ablations).

The results show no significant differences between the experimental and the normal animals in any measured aspect of the performance required by our tests. The experimental animals responded to similarities (between the test objects and the training objects), and shifted from one cue or category to another, with as much facility as did the normal animals. None of the four subjects was dependent on the original, complete, and unaltered pattern of stimulation. Each animal, both experimental and control, responded to each of three component properties of the training objects, presented singly, with an accuracy significantly above chance.

Since the "abstract attitude" is defined so broadly, including functions which may or may not be tapped by our tests, it seems desirable to characterize the results more strictly with reference to the test requirements. Success on the single-cue tests requires response to each of the component aspects of the original multiple-cue pattern (i. e., response to sensory similarity or partial identity), recognition of these aspects in new contexts (i. e., independence from the "concrete uniqueness" of the training objects), and ability to shift responsiveness from one aspect to another as required (plasticity versus rigidity of perceptual responsiveness). These requirements add up to something more than the second type of Bolles' "bases of pertinence" and correspond to what is usually understood by abstraction, or more specifically, sensory abstraction.[20]

The sorting and matching tests may involve different degrees of the aforementioned abilities, or perhaps additional abilities; our results, therefore, should not be extrapolated to predict absence of impairment in those performances. The reduced-cue test does not involve the "Weigl principle" as this pertains to the conditional matching problem; nor does it involve, in any obvious fashion, those capacities which have been suggested as critical for delayed response.

The operations for ablation of prefrontal cortex in our two experimental subjects were made at a relatively early age (2 months). According to Hebb's neuro-

20. Nissen, H. W.: Phylogenetic Comparison, in Stevens, S. S., Editor: Handbook of Experimental Psychology, New York, John Wiley & Sons, Inc., 1951, p. 374 ff. Revesz, G.: Abstraction in Monkeys, J. Comp. Psychol. **5**:293-343, 1925.

psychological theory, "an early injury may prevent the development of some intellectual capacities that an equally extensive injury, at maturity, would not have destroyed.[21]" The fact that our experimental animals showed no behavioral deficit suggests that establishment of the particular capacity required by our tests does not involve the prefrontal cortex. Since we have not similarly tested animals operated on at a later age, our results have no implications for the opposing view, namely, that the cortex loses in plasticity or adaptivity with age, and that therefore remaining portions of the brain become progressively less able to take over functions lost by operation.[22]

Response to Frustration.—Records were made, during or after each experimental session, of the occurrence of screaming, temper tantrums, aggressive behavior toward the apparatus or experimenter, and amount of gross activity between trials. Response latencies (time elapsing between presentation of the stimulus objects and the displacement of one of them) were recorded during the latter part of the study.

Frequency and intensity of the aforementioned emotional expressions were very much greater in the two experimental subjects than in the two (normal) controls. In general, such behavior occurred predominantly after errors, especially after a number of successive nonrewarded responses. The expression of frustration was most frequent and violent during the first sessions following a change in procedure, i. e., at the beginning of Steps 2, 3, and 4. As a given procedure was continued, e. g., in the 20 sessions of Step 2, there was a decrease of emotional responsiveness concomitant with a decrease of errors. Alan's (Op) response to frustration took the form of loud screaming, slapping at the stimulus objects, and heightened activity between trials. Ked (Op) typically whimpered or screamed, sucked his thumb, and had long response latencies. Verb (N) was quiet and calm, and responded promptly, throughout the experiment. Dehn (N) became violently aggressive toward the apparatus during the first two sessions of Step 3, but otherwise worked quietly and rapidly.

It is clear that these observations do not indicate any diminution of emotional expression in our animals with prefrontal ablations. It is important, however, to distinguish between overt expressions of emotion, as may be seen in the outward behavior of animals and men, and verbal reports of subjective mood or feeling. After lobotomy for intractable pain, for instance, the human patient may be even more subject to outbursts of rage and assaultiveness than before, and yet he may report that his pain is more bearable, his feelings less intense. Putting our reliance

21. Hebb, D. O.: The Organization of Behavior: A Neuropsychological Theory, New York, John Wiley & Sons, Inc., 1949, p. 292.

22. Three other laboratory chimpanzees underwent ablation of the prefrontal lobes several years earlier. One was an adult; the others were about 6 years old at the time of operation. The performance of all three in spatial delayed response was significant above chance, with delays of one minute or longer. In addition, one of them showed excellent retention for generalized matching and did well in spatial delayed matching. (These three animals were not given the reduced-cue tests used in the present study.) The foregoing observations were made by Robert A. Blum and are reported in his doctoral thesis (Nature of Delayed Response Deficit in Relation to Locus and Character of Prefrontal Extirpations in Primates, Thesis, Yale University, 1949). Dr. Blum found some increase of activity "under conditions of excitement" in one subject, but no diminution of "emotional reactivity to disturbing or frustrating situations."

mainly on the verbal statements, we judge that there has been a "flattening" of the emotions. The chimpanzee, of course, cannot give us introspective reports of his feeling states. It may be, therefore, that in animal, as in man, the less controlled and more violent behavior is accompanied by a diminished intensity of feeling. It should be noted, also, that the greater emotional expressiveness of our experimental subjects, as compared with the control animals, may be related to the somewhat greater age of the latter. Finch [23] has shown that the frustration responses of chimpanzees become less violent with increasing age. Again, it may be that decreased expressivity with age, which seems to be true of man also, is an unreliable index of subjective mood.

SUMMARY

The subjects of this study were two chimpanzees that had undergone bilateral ablation of the prefrontal cortex at the age of 2 months and two normal (control) animals. All four animals were trained on a three-cue discrimination problem and were then tested with pairs of objects each of which presented only one of the stimulus differences. Subsequently, the animals were trained on the reverse of the original discrimination and were then given single-cue tests based on the reversed habit. It is suggested that the single-cue tests provide an index of sensory abstraction, which is probably the principal function tapped by the sorting tests often used with human patients as a measure of the "abstract attitude." No significant differences between the experimental and the normal subjects were found in the reduced-cue tests, initial learning, or reversed learning. All four animals were able to discriminate on the basis of the component properties of the training stimuli.

The two animals with prefrontal ablations gave more frequent and more violent emotional expression to the frustration of failure than did the slightly older control subjects.

23. Finch, G.: Chimpanzee Frustration Responses, Psychosom. Med. **4**:233-251, 1942.

POLIOMYELITIS

VIII. Studies on Temperature Regulation

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AND

SAM CORNWELL

MINNEAPOLIS

THE MAINTENANCE of a constant body temperature is dependent upon two distinct bodily functions, heat production and heat loss. The balance between these two mechanisms maintains the body at optimum temperature. An undue fall in body temperature is brought about by a reduction of metabolic heat, as well as the actuation of such processes as sweating and dilatation of cutaneous vessels. Heat production results from an increase in metabolism, as well as such mechanisms as shivering and constriction of cutaneous vessels. That these two mechanisms are structurally distinct has been shown by studies in which one has been eliminated, leaving the other intact (Keller,[1] Bazett,[2] Alpers,[3] Teague and Ranson,[4] and Ranson and associates[5]).

Tscheschichin[6] was the first to insist that there was a definite heat center somewhere above the medulla. In 1885 Aronsohn and Sachs[7] first called attention to a possible heat center in the corpus striatum, and a number of investigators by means of experimental studies confirmed his observations (White,[8] Aisenstat,[9]

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1. Keller, A. D.: Separation in the Brain Stem of the Mechanisms of Heat Loss from Those of Heat Production, J. Neurophysiol. **1**:543, 1938.

2. Bazett, H. C.: Further Experiments on Chronic Decerebrate Cats, Am. J. Physiol. **101**:5, 1932.

3. Alpers, B. J.: Hyperthermia Due to Lesions in the Hypothalamus, Arch. Neurol. & Psychiat. **35**:30, 1936.

4. Teague, R. S., and Ranson, S. W.: Role of the Anterior Hypothalamus in Temperature Regulation, Am. J. Physiol. **117**:562, 1936.

5. Ranson, S. W.; Fisher, C., and Ingram, W. R.: Hypothalamic Regulation of Temperature in the Monkey, Arch. Neurol. & Psychiat. **38**:445, 1937.

6. Tscheschichin, J.: Zum Lehre von der thierischen Wärme, Arch. Physiol. p. 151, 1866.

7. Aronsohn, E., and Sachs, J.: Die Beziehungen des Gehirns zur Körperwäarme und zum Fieber: Experimentelle Untersuchungen, Arch. ges. Physiol. **37**:232, 1885.

8. White, W. H.: Report on the Position and Relative Value of Such Lesions of the Brain as Cause an Alteration of the Bodily Temperature, Brit. M. J. **1**:569, 1891.

9. Aisenstat, M.: Die Lage der Wärmezentren des Kaninchens und das Erkennen der Lage derselben durch äussere Merkmale, Arch. Physiol., p. 475, 1909.

Nikolaides and Dontas,[10] Barbour,[11] Barbour and Wing,[12] Ott[13]). More recent investigations, however, have failed to confirm these observations (Sachs and Green,[14] Moore,[15] Clark and associates[16]). Moore injured the caudate nucleus of rabbits but produced no change in body temperature in 75% of the animals. Clark and his associates produced lesions within the thalamus with a Horsley-Clark apparatus with little disturbance in temperature regulation.

The brain tissue above the corpus striatum has also been investigated and found to play little role in the regulation of temperature. Dusser de Barenne[17] removed all the brain above the thalamus in cats and noted no loss of temperature control. Pinkston and associates[18] observed that cats and dogs retained their ability to regulate body temperature in the presence of cerebral damage provided the hypothalamus was intact.

Most of the more recent studies have established the importance of the hypothalamus for regulation of temperature, but there is still a great difference of opinion as to the exact location of the centers involved. The present study of the hypothalamus in cases of bulbar poliomyelitis with hyperthermia or hypothermia was undertaken in an attempt to throw further light on this problem.

HYPERTHERMIA

Neurogenic hyperthermia has been observed to follow operative procedures on the pituitary fossa, the region of the third ventricle, or the posterior fossa. A number of experimental studies have been undertaken to localize this controlling area within the hypothalamus. Most investigators have shown that damage to the anterior hypothalamus results in hyperthermia, but the exact part of the hypothalamus that must be injured is still questionable. Frazier, Alpers, and Lewy[19] and Bazett, Alpers, and Erb[20] produced destructive hypothalamic lesions in cats and concluded

10. Nikolaides, R., and Dontas, S.: Wärmezentrum und Wärmepolypnoe, Arch. Physiol. p. 249, 1911.

11. Barbour, H. G.: Die Wirkung unmittelbarer Erwärmung und Abkühlung der Wärmezentra auf die Körpertemperatur, Arch. exper. Path. u. Pharmakol. **70**:1, 1912.

12. Barbour, H. G., and Wing, E. S.: Direct Application of Drugs to the Temperature Centers, J. Pharmacol. & Exper. Therap. **5**:105, 1913.

13. Ott, I.: Inter-Brain: Its Relation to Thermotaxis, Polypnœa, Vaso-Dilatation and Convulsive Action, J. Nerv. & Ment. Dis. **18**:433, 1891.

14. Sachs, E., and Green, P. P.: Further Observations on Cerebral Heat Centers, Am. J. Physiol. **42**:603, 1917.

15. Moore, L. M.: Experimental Studies on the Regulation of Body Temperature: II. Relation of the Corpus Striatum to the Regulation of Body Temperature, Am. J. Physiol. **46**:253, 1918.

16. Clark, G.; Magoun, H. W., and Ranson, S. W.: Temperature Regulation in Cats with Thalamic Lesions, J. Neurophysiol. **2**:202, 1939.

17. Dusser de Barenne, J. G.: Recherches expérimentales sur les fonctions du système nerveux central, faites en particulier sur deux chats dont le néopallium avait été enlevé, Arch. néerl. physiol. **4**:31, 1919.

18. Pinkston, J. O.; Bard, P., and Rioch, D. M.: Responses to Changes in Environmental Temperature After Removal of Portions of the Forebrain, Am. J. Physiol. **109**:515, 1934.

19. Frazier, C. H.; Alpers, B. J., and Lewy, F. H.: Anatomical Localization of the Hypothalamic Center for the Regulation of Temperature, Brain **59**:122, 1936.

20. Bazett, H. C.; Alpers, B. J., and Erb, W. H.: Hypothalamus and Temperature Control, Arch. Neurol. & Psychiat. **30**:728, 1933.

that if the lesions were placed bilaterally and medially in the floor of the third ventricle, destroying the substantia grisea, the animals became thermolabile with a particular disturbance in their cooling mechanism. Ranson and his associates (Teague and Ranson [4]; Clark, Magoun, and Ranson [16]) observed that medially placed lesions in the anterior hypothalamus of cats produced only a transitory elevation of temperature. Lesions in the lateral part of the anterior hypothalamus resulted in immediate and lasting hyperthermia. Ranson, Fisher, and Ingram [5] repeated these studies on monkeys and observed that hyperthermia resulted only when the lesions involved the rostral part of the lateral hypothalamic area and the region around the formix. The ventromedial, paraventricular, supraoptic, and suprachiasmatic nuclei were intact.

A number of cases of hyperthermia have been reported in man as a result of lesions in the hypothalamus. Alpers [3] and Zimmerman [21] reported cases of tumors affecting the rostral and medial areas of the hypothalamus, with resulting hyperthermia. In Alpers' cases the lesions were located in the substantia grisea with destruction of the adjacent tuber cinereum; in Zimmerman's cases the ventromedial nuclei were involved. Davison [22] studied four cases of hyperthermia in which a tumor involved the anterior hypothalamus but implicated both the medial and the lateral area. Chiefly the preoptic and supraoptic regions were damaged, but in some cases also the paraventricular, the medial, and the lateral nuclei. Strauss and Globus [23] reported three cases in which tumors situated chiefly in the lateral hypothalamus but also invading the periventricular nuclei resulted in hyperthermia. Such clinical studies are interesting, but the extensiveness of the lesions, with the associated tissue changes, does not allow for an accurate localization of the pathologic process producing the temperature disturbances. Morgan and Vonderahe [24] studied 13 cases of heat stroke. They found the severest cell damage within the paraventricular nucleus and the nucleus tuberalis. They were of the opinion that the larger cells of the more anteriorly placed paraventricular and tuberal nuclei were concerned with elimination of heat and that their injury resulted in hyperthermia.

Present Study.—During the years 1946 to 1949 complete autopsies were obtained in 115 cases of bulbar poliomyelitis, and the hypothalamus was studied in detail in each case (Baker, Cornwell, and Brown [25]). The hypothalamus was divided into three levels, and the principal nuclear groups were studied as follows: (*a*) the supraoptic, periventricular, and tuberal nuclei, in the anterior hypothalamus, at the level of the optic chiasm; (*b*) the dorsomedial, ventromedial, and lateral nuclei, in the middle hypothalamus, at the level of the tuber cinereum, and (*c*) the posterior and mamillary nuclei, in the posterior hypothalamus, at the level of the mamillary body. In a previous publication [25] the changes within these hypothalamic

21. Zimmerman, H. M.: Temperature Disturbances and the Hypothalamus, A. Res. Nerv. & Ment. Dis., Proc. **20**:824, 1940.

22. Davison, C.: Disturbances of Temperature Regulation in Man, A. Res. Nerv. & Ment. Dis., Proc. **20**:774, 1940.

23. Strauss, I., and Globus, J. H.: Tumor of the Brain with Disturbance in Temperature Regulation, Arch. Neurol. & Psychiat. **25**:506, 1931.

24. Morgan, L. D., and Vonderhe, A. R.: Hypothalamic Nuclei in Heat Stroke, with Notes on Central Representation of Temperature Regulation, Arch. Neurol. & Psychiat. **42**:83, 1939.

25. Baker, A. B.; Cornwell, S., and Brown, I. A.: Poliomyelitis: VI. The Hypothalamus, A. M. A. Arch. Neurol. & Psychiat. **68**:16, 1952.

nuclear groups were described, and an attempt was made to correlate such changes with the clinical symptoms and signs presented by the patients. During the course of that study it was observed that a number of patients manifested an unusual hypothermia or a hyperthermia. It was felt that a more careful study of the cases might offer some information on the role of the hypothalamus in the control of body temperature. The method of study and the normal structure of the hypothalamic nuclei have already been described,[25] and the reader is referred to the previous publication for these details.

In patients acutely ill with a severe infection, often complicated by pulmonary or urinary involvement, evaluation of the significance of a hyperthermia is often difficult. Most patients with bulbar poliomyelitis have a very high terminal temperature, and many have a fairly high temperature at the onset of their illness. However, in a number of our cases the hyperthermia was out of proportion to the severity of the illness and often comprised the predominant symptom. In some patients the hyperthermia continued throughout the illness and resisted all efforts at reduction.

TABLE 1.—*Percentage of Cell Damage in Hypothalamic Nuclei in Twelve Cases of Fatal Bulbar Poliomyelitis with Hyperthermia*

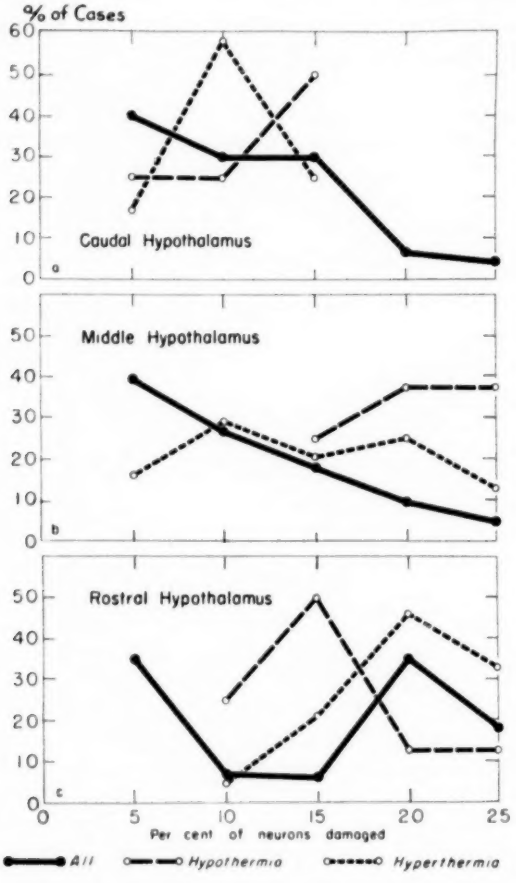
Patient	Paraventricular	Supraoptic	Tuberal	Lateral	Medial	Posterior	Mamillary
K. C.	15	15	5	9	5	5	0
R. B.	5	15	5	5	5	5	0
M. S.	10	15	8	10	0	0	0
M. E.	15	20	5	15	10	10	0
W. F.	15	25	0	20	15	12	0
O. T.	15	25	0	15	5	0	0
A. S.	10	10	0	10	0	5	0
D. W.	15	20	0	15	10	10	5
D. K.	18	15	0	20	0	5	5
C. H.	5	15	0	15	5	5	0
R. G.	10	10	5	10	5	5	0
J. J.	10	15	0	15	0	5	5
Average	11.7	16.7	5.6	13.3	7.5	6.7	5.0
Average for all 115 cases of bulbar poliomyelitis	6.9	12.0	2.21	8.8	8.0	8.0	1.0

Many of these patients showed no evidence of any secondary infection which might have accounted for the elevated temperature. In order to establish fairly rigid standards in selecting our cases of abnormal hyperthermia, we used the following criteria: (1) an acute onset of very high fever after a period of relatively moderate hyperthermia; (2) persistence of the hyperthermia throughout the illness in spite of subsidence of other clinical evidence of the acute illness; (3) absence of any evidence of pulmonary or urinary pathology. Twelve cases were selected which appeared clinically to fit these criteria and in which the entire hypothalamus was available for study (Table 1).

A diffuse interstitial cell reaction was present in all 12 cases. This inflammatory reaction was both diffuse and perivascular but did not produce any destruction of the underlying tissues. In contrast to the entire group of cases of bulbar poliomyelitis, in which the inflammatory process was less intense in the rostral portion of the hypothalamus, in the cases of hyperthermia the mesodermal-glial reaction was most intense in the anterior and middle portions of the hypothalamus, extending laterally

to implicate the lateral areas. The supraoptic, paraventricular, and lateral nuclear groups, particularly, showed a fairly intense inflammatory process. The posterior, tuberal, and mamillary nuclei revealed only minimal evidence of inflammation.

Neuronal Changes: Because of the normal variations in the structure of the hypothalamic nuclei, fairly rigid criteria were accepted as indicators of neuronal damage in our studies. The following changes only were accepted as abnormal:



Percentage of cell damage at the various levels of the hypothalamus in cases of hypothermia and hyperthermia associated with poliomyelitis, as compared with the cell damage in all cases of bulbar poliomyelitis.

complete chromatolysis, ghost cell formation, neuronophagia, cell fragmentation, and extrusion of the nucleus. With use of these criteria, the percentage of cell damage in each of the nuclear groups in our cases of hyperthermia have been listed in Table 1. The severity of the cell damage in the various regions of the hypothalamus are illustrated in the accompanying chart.

In fatal cases of bulbar poliomyelitis in which clinical evidence of hyperthermia was manifested, the cell damage was much more intense in the rostral hypothalamus, implicating primarily the paraventricular, the supraoptic, and the lateral nuclei (Chart; Table 1). The medial and posterior cell groups revealed only minimal changes and showed no increase in damage over that in cases without hyperthermia.

It would appear, therefore, that three nuclear groups may play a role in the reduction of body temperature, namely, the supraoptic, the paraventricular, and the lateral. In an attempt to evaluate further the specificity of these nuclei in the regulation of body temperature, a histologic study was made of these three nuclear groups in all our cases of bulbar poliomyelitis in order to determine whether severe damage existed when there was no clinical history of an abnormal elevation of temperature.

Supraoptic nucleus. In 38 of our cases the supraoptic nucleus showed unusually severe involvement. In 24 cases the cell damage varied from 15 to 20%, while in the remaining 12 cases over 20% of the cells were destroyed. In only 10 of the 36

TABLE 2.—*Percentage of Severe Cell Damage to Supraoptic Nucleus in Cases of Poliomyelitis Without Hyperthermia*

Patient	Paraventricular	Supraoptic	Tuberal	Medial	Lateral	Posterior	Mamillary
R. D.	9	15	5	15	8	5	5
E. W.	5	17	5	14	6	0	5
J. S.	8	15	5	8	5	0	5
C. J.	8	18	0	15	14	0	5
J. J.	6	16	12	8	11	16	5
F. W.	0	15	5	5	5	0	0
M. J.	7	16	5	16	13	5	0
Wm. M.	15	20	8	10	10	6	0
S. S.	8	25	5	6	8	5	0
W. O.	13	22	12	10	16	0	5
D. H.	6	22	6	6	9	12	5
V. C.	8	15	5	6	5	5	0

cases were those criteria which we had outlined for hyperthermia considered to have been manifested clinically. The case histories of the remaining 28 cases which were not considered typical of or satisfactory for hyperthermia were reviewed and divided into four groups: (1) 12 in which the temperature remained below 103 F.; (2) 4 in which there was only a terminal rise of temperature above 103 F.; (3) 8 in which there was a marked hyperthermia but the course of the illness was too fulminating to permit proper evaluation of the significance of this hyperthermia, and (4) 4 in which hyperthermia occurred but severe pulmonary infection that might have caused the rise in temperature was also present.

It is possible that the last three groups, consisting of 16 patients, might well represent cases of hyperthermia in spite of the clinical difficulties in so classifying them. However, this would still leave the 12 cases in Group 1 in which severe destruction of the supraoptic nucleus occurred and at no time was there any unusual elevation of temperature (Table 2). It might be postulated in these cases that damage to the middle or posterior hypothalamus (which is believed to play a role in the elevation of body temperature) might neutralize or cover any specific alterations in temperature resulting from injury to the anterior hypothalamus. However,

as Table 2 indicates, in none of these cases was any excessive damage to the posterior hypothalamic nuclei revealed. The medial nuclei, although very severely damaged in some cases, were only mildly implicated in others.

From these observations it would appear that the supraoptic nucleus, although often severely damaged in cases of hyperthermia, actually plays little specific role in the regulation of temperature.

Paraventricular nucleus. In all the 115 cases of bulbar poliomyelitis this nuclear group revealed an average cell damage of 6.9%, whereas in cases with hyperthermia there occurred an average cell damage of 11.7%. In a review of the damage of this nuclear group in all our cases, severe involvement was found in 20. Twelve of these were classified as cases of hyperthermia. The clinical histories of the remaining eight cases were reviewed to determine the possible specificity of this nucleus in control of temperature. In all but one of these eight cases the temperature during or at the end of the illness was above 103 F. In most cases the temperature ranged from 104 to 106 F. However, these seven cases were not included in our series of cases of hyperthermia because the course of the illness was too acute and it was, therefore, impossible to determine whether the elevation of temperature was due to the acute illness or to hypothalamic damage. In the only exception, the patient had a prolonged illness, lasting 22 days, and died of pulmonary abscesses. In this case there was extensive damage to both the paraventricular and the medial nuclei. As will be seen in our studies on hypothermia, the medial nuclei are probably essential in the elevation of body temperature. It is possible, therefore, that damage to the medial nuclear group was important in neutralizing the effect of damage to the anterior hypothalamus and prevented a rise in body temperature in spite of damage to the latter.

Lateral nuclei. This nuclear group generally shows about 8.8% damage in cases of bulbar poliomyelitis (Table 1). In cases with hyperthermia the cell damage is severer, averaging about 13.3%. In 24 of our cases of bulbar poliomyelitis examination revealed actual extensive damage to the lateral nuclei. In 12 of these cases there was clinical evidence of hyperthermia, leaving 12 other cases unaccounted for. A review of these case histories revealed markedly elevated temperatures in nine, but the illness was too acute for their inclusion in the study. In three cases, in spite of extensive damage to the lateral nuclei (14, 15, and 13%), no abnormal elevation of temperature was present. In two of these cases there was even an associated severe pulmonary pathology. In none of the latter three cases was there any unusual involvement of the posterior hypothalamus; however, in all cases the medial nuclei revealed severe damage (14, 15, and 16%), again suggesting that involvement of this nuclear group may play an important role in preventing an elevation of body temperature which normally results from damage to the anterior hypothalamus.

Comment.—A correlation of the damage to the individual hypothalamic nuclei with the clinical appearance of hyperthermia reveals that three cell groups may play a role, namely, the supraoptic, the paraventricular, and the lateral. Since all these groups are situated in the anterior hypothalamus, one seems justified in concluding that the anterior hypothalamus is active in reducing body temperature and that its injury will allow the development of hyperthermia. These observations are consistent with those already recorded in the literature. Any attempt to determine whether any single nuclear group plays a predominant role in temperature control

is somewhat more difficult. The supraoptic nucleus, although the most severely damaged of all nuclear groups in cases of hyperthermia, is also extensively damaged in many patients who show no temperature disturbances (Table 1). Certainly, such studies would tend to indicate that this structure probably plays little part in temperature control. This leaves only the paraventricular and lateral nuclei, both of which appear to be important in regulating heat loss and preventing hyperthermia. In all but three cases in which these structures were damaged hyperthermia was manifested, and in these three the severe involvement of the medial nuclei may well have neutralized the effect of the injury to these nuclei. These observations tend to substantiate the observations of Morgan and Vonderahe,[24] who found the paraventricular nuclei most severely damaged in patients with heat stroke manifesting severe hyperthermia.

HYPOTHERMIA

Hypothermia is usually not as striking or as common a clinical phenomenon as is hyperthermia, even though a number of interesting cases have been reported in the literature. For some time experimental studies have suggested the important role of the hypothalamus in regulating heat loss and in preventing abnormal rises in body temperature. As early as 1888 Sawadowski [26] induced lowering of body temperature by transection of the brain stem in the region of the thalamus and pons. Similar observations were made by Lewzisky [27] and by Bazett and associates [29] suggesting that fibers controlling the "heating mechanism" apparently descended in the brain stem from higher centers. In 1914 Isenschmid and Schnitzler [28] showed that small bilateral lesions in the region of the mamillary bodies and the posterior part of the tuber cinereum resulted in loss of capacity to prevent abnormal drops in body temperature. Most investigators seem to agree that the posterior hypothalamus plays an important role in maintaining body temperature and that injury to this region will result in hypothermia. Ranson and his associates [29] placed lesions in the hypothalamus of cats with the Horsley-Clark apparatus and observed that laterally placed lesions in the posterior hypothalamus caused an impairment in ability to regulate against cold, resulting in hypothermia; medially placed lesions in the posterior hypothalamus caused little disturbance in temperature regulation. Ranson, Fisher, and Ingram [5] reported similar observations in monkeys. They produced hypothermia in 13 monkeys and in all the animals the lesions had destroyed the region dorsal and lateral to the rostral end of the mamillary bodies, implicating the lateral and posterior hypothalamic nuclei. The nuclei anterior to the mamillary bodies were intact, as were the medial portions of the rostral hypothalamus. No attempt was made to identify special cell groups that may play a more important role in maintaining body temperature.

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26. Sawadowski, J.: Zur Frage über die Lokalisation der Wärmeregulirenden Centren im Gehrin und über die Wirkung des Antipyrins auf den Tierkörper, Centralbl. med. Wissensch. **26**:145, 1888.

27. Lewzisky, P.: Über den Einfluss des schwefelsäuren Chinins auf die Temperatur und Blutcirculation, Arch. path. Anat. **47**:352, 1869.

28. Isenschmid, R., and Schnitzler, W.: Beitrag zur Lokalisation des der Wärmeregulation vorstehenden Zentralapparates im Zwischenhirn, Arch. exper. Path. u. Pharmakol. **76**:202, 1914.

29. Teague and Ranson,[4] Clark, Magoun, and Ranson.[16]

Very few clinical reports of hypothermia have appeared. Ratner [30] studied a case in which a meningioma involved the inferior temporal lobe and the hippocampus, reaching as far as the walls of the third ventricle. The patient had a temperature of 96.4 F. Obregia and associates [31] reported a case of hypothermia in a patient with a craniopharyngioma compressing the floor of the third ventricle. Zimmerman [21] recorded a case in which there was calcification of the posterolateral group of hypothalamic nuclei. The anteriorly situated nuclei were intact. Davison [22] made similar observations. In a series of four cases with abnormally low body temperatures, tumors had destroyed the caudal portion of the hypothalamus, chiefly the lateral area. In some cases the anterior and middle hypothalamic areas were also damaged. Davison and Selby [32] studied the hypothalamus in a patient with an angioma above the sella turcica who manifested hypothermia. The nucleus tuberalis was completely destroyed, while the mamillary, the posterior, and the supraoptic nuclei were only slightly damaged. They concluded that hypothermia was due to destruction of the nucleus tuberalis and that this nuclear group plays an important role in heat production.

TABLE 3.—*Percentage of Cell Damage in Cases with Hypothermia*

Patient	Paraventricular	Supraoptic	Tuberal	Lateral	Medial	Posterior	Mamillary
L. E.	5	15	0±	15	18	0	0
W. W.	15	20	5	20	20	10	5
V. B.	5	10	0±	15	10	10	5
K. P.	16	12	0	15	10	5	0
Average	8.8	14.2	1.2	16.3	14.5	6.2	1.2
Average for all cases of bulbar poliomyelitis	6.9	12.0	2.3	8.8	8.0	8.0	1.0

Present Study.—Hypothermia is much more difficult to evaluate clinically than is hyperthermia. It is possible that many patients with bulbar poliomyelitis complicated by severe pulmonary infection who show only a mild rise in temperature may actually be manifesting some degree of hypothermia. However, it was considered inadvisable to include such cases in this study. Because of the rigid criterion set up for hypothermia, that is, an actual subnormal temperature, only four cases were accepted in this study. The percentages of hypothalamic cell damage in these cases are given in Table 3.

Only two nuclear groups showed unusually severe damage in all cases of hypothermia, namely, the lateral and the medial. Since the lateral nucleus was also severely damaged in cases of hyperthermia, it probably does not play a specific role in raising body temperature. It may, nevertheless, be important in the mechanism of control of body temperature.

30. Ratner, J.: Tumor des Mittelhirns unter dem Bilde einer pluriglandulären Insuffizienz, Klin. Wchnschr. **4**:599, 1925.

31. Obregia, A.; Dimolescu, A., and Constantinescu, S.: Syndrome infundibulo-tubérien avec troubles mentaux complexes par tumeur supra-sellaire due troisième ventricule: Étude anatomo-clinique, Encéphale **27**:93, 1932.

32. Davison, C., and Selby, N. E.: Hypothermia in Cases of Hypothalamic Lesions, Arch. Neurol. & Psychiat. **33**:570, 1935.

The medial nuclei of the hypothalamus, on the other hand, would appear to be much more specifically involved in cases of hypothermia. In order to check this impression we rechecked all cases of bulbar poliomyelitis to determine in how many there was severe damage to the medial nuclei comparable to that seen in cases of hypothermia. A total of 10 cases were found in which the medial hypothalamic nuclei revealed damage to at least 14% of its cell elements. Of these 10 cases, 4 were already included as cases of hypothermia. In all but one of the remaining six cases the temperatures ranged only from 98.6 to 101 F. in spite of a severe acute illness and/or severe terminal pulmonary infections, such as pneumonia, and even lung abscesses. A report of two illustrative cases may be helpful.

CASE 1.—A boy aged 4 years first became ill with sore throat and a mild elevation of temperature, which persisted for the next few days, when dysphagia developed. When admitted two days after the onset of his illness, the patient was acutely ill and had a temperature of 104 F., stiff neck, and dysphagia. He remained critically ill throughout his hospital stay. A pronounced lethargy and drop in blood pressure developed. In spite of the continued acuteness of his illness, the temperature dropped to 99 F. during the first hospital day and remained between 98 and 100 F. throughout the seven remaining days of life. Autopsy revealed severe pneumonia involving both lungs, in addition to the pathology of the nervous system. Studies of the hypothalamus revealed minimal alterations within all nuclear groups except the lateral and medial, which showed 15 and 14% cell damage respectively.

CASE 2.—A youth aged 15 had a history of abdominal pain, anorexia, fever, and nuchal rigidity of eight days' duration. On admission, his temperature was 101.4 F.; his white blood cell count, 13,300, and his spinal fluid cell count, 74, per cubic millimeter. He had paralysis of both arms and scattered involvement of the cranial nerves. During the first eight days in the hospital he was somewhat lethargic and had some difficulty with respiration. He was placed in a respirator, and a tracheotomy was performed. During the next 12 days the patient seemed to improve and was able to remain out of the respirator for long periods. Two days before his death he took a turn for the worse; he died suddenly, of a circulatory collapse. Throughout his hospital stay, of 22 days, his temperature fluctuated between 98.6 and 101 F., ranging mostly around 99 to 100 F. Autopsy revealed multiple abscesses and scattered areas of consolidation in both lungs. Within the hypothalamus only the medial nuclei showed severe damage, 15% of the nerve cells being damaged.

In all these cases of hypothermia the severity of the illness and the serious secondary complications should have resulted in very high temperatures, particularly during the terminal phases. However, the temperature remained low, even terminally, suggesting definite impairment of that mechanism which regulates body heating. In view of the relatively low temperatures, these cases could justifiably be considered instances of relative hypothermia. It would appear, therefore, that the medial nuclei of the hypothalamus are closely related to elevation of body temperature and that their destruction will result in low or subnormal body temperatures.

CONCLUSIONS

A clinicopathologic study of the hypothalamus was undertaken in 115 cases of bulbar poliomyelitis to determine whether any of the cell groups were specific in the regulation of body temperature.

In 12 cases a definite prolonged hyperthermia was manifested. In all these cases the cell damage was severest in the rostral portion of the hypothalamus, implicating chiefly the supraoptic, paraventricular, and lateral nuclei. Of these nuclei, only

severe damage to the paraventricular nuclei was exclusively associated with excessive temperature elevations, and this group was believed to play a most important role normally in the lowering of body temperature.

In nine cases a definite or a relative hypothermia was revealed clinically. In all these cases the lateral and the medial hypothalamic nuclei were severely damaged. Since the lateral nuclei were also injured in cases of hyperthermia, only the medial cell group was considered specific for elevation of body temperature, with damage to this nuclear group resulting in hypothermia.

The lateral hypothalamic nuclei were severely damaged in patients showing both very high and abnormally low body temperatures. These nuclei would appear to play a very important accessory role in the regulation of body temperature, and their damage apparently produces poikilothermia, with either abnormal heating or cooling resulting.

The posterior hypothalamic nuclei were not severely involved in any of our cases of bulbar poliomyelitis with unusual temperature disturbances. From the results of our studies, this area does not appear to participate in the regulation of body temperature.

Because of the frequent involvement of the hypothalamus in bulbar poliomyelitis, resulting in an instability in temperature control, particular care must be given to the regulation of body temperature in all patients with bulbar poliomyelitis in order to prevent or to minimize excessive temperature elevations, which may complicate the care of these acutely ill patients.

SUBARACHNOID INJECTION OF ALCOHOL IN TREATMENT OF SPASTICITY IN PARAPLEGIA

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THE SPASTICITY which all too frequently accompanies lesions of the spinal cord is itself a disabling and, in fact, an incapacitating symptom over and above the effects of the original lesion. It is highly annoying to the patient, who at any time may be thrown into a violent muscular spasm, often associated with involuntary defecation, urination, and erection. In addition, it hinders ambulation and is an obstacle in the way of proper nursing care. It has also been thought to be a factor in the production and maintenance of decubitus ulcers. Until the introduction of anterior rhizotomy, there was no known method of adequately relieving the spasticity of paraplegia. Revision of the injured portions of the spinal cord, posterior rhizotomy, operations on the sympathetic nervous system, and medical treatment of all kinds had failed to give relief. Anterior rhizotomy was not always feasible, since the patient was often not in condition to stand a major operation. In addition, technical difficulties in the way of identifying the proper roots to be sectioned many times made the operation at least a partial failure. With the advent of subarachnoid alcohol block, as first described by Boucher [1] and Shelden and Bors [2] in 1948, and confirmed by Cooper and Hoen [3] in 1949, a simple, safe, and effective method became available everywhere. It is clear, however, that knowledge of this method has not yet become widespread and that many patients are being allowed to continue in a highly spastic state, either permanently or for a much longer period than necessary. The neurosurgeon is often not called to see such a patient because it is clear to the referring physician that no major operation could be undertaken. This is due, however, to the practitioner's thinking in terms of anterior rhizotomy or other major surgical procedure.

Although intrathecal, and even intraspinal injection of alcohol had been used before, the amount injected had been much too small to produce the desired result. When partial relief was obtained, it proved, in addition, to be but temporary. Boucher [1] reported some 60 cases in which absolute alcohol was injected into the subarachnoid space with the patient prone. After the injection the head was imme-

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1. Boucher, R.: De l'injection intrarachidienne d'alcool absolu dans les cas de paraplégie spasmodique, Bull. Acad. nat. méd. **132**:362 (May 25-June 1) 1948.

2. Shelden, C. H., and Bors, E.: Subarachnoid Alcohol Block in Paraplegia: Its Beneficial Effect on Mass Reflexes and Bladder Dysfunction, J. Neurosurg. **5**:385 (July) 1948.

3. Cooper, I. S., and Hoen, T. I.: Intrathecal Alcohol in the Treatment of Spastic Paraplegia, J. Neurosurg. **6**:187 (May) 1949.

diately lowered. The spasms were said to be relieved, allowing for the easier treatment of decubitus ulcers and bladder infections and making for easier ambulation. Postinjection headaches occurred in four cases, and these were said to yield to injection of dextrose solution. Encouraging comment was made on this paper by Lhermitte. Sheldon and Bors [2] and Cooper and Hoen [3] began almost simultaneously and independently to experiment with subarachnoid injection of alcohol in larger amounts. Both groups of investigators obtained excellent results. Shelden and Bors, in their article, referred to the prior use of "large amounts of alcohol" by Pudenz and Nourse. These data had not yet been published. Shelden and Bors selected only patients who had no voluntary bladder function or automaticity. The patient was placed on his side in the usual position for lumbar puncture, and 10 to 15 cc. of absolute alcohol was injected into the lumbar sac. He was then quickly turned on to his back, and his hips were kept elevated for 24 hours. The authors reported on 24 cases. The longest follow-up study was 15 months. All the patients were relieved of spasticity. Sixteen had had a hypotonic bladder. Twelve of these had urinary retention, and the other 4 had large residuals. All but one were relieved of retention. In all eight patients with hypertonic bladder voluntary micturition and increased bladder capacity developed after the alcohol block. Their previous status was not mentioned. Twenty-two of the 24 patients lost their ability to have erections. Cooper and Hoen reported eight cases with a follow-up study of 12 to 18 months. One patient died of urinary infection; one had a sufficient return of spasticity to warrant further measures. All six remaining patients had complete relief. Six patients had hypertonic bladders which became atonic and automatic after the block. Cooper and Hoen used 7 to 12 cc. of 95% alcohol, injected at a rate of 1 cc. per minute.

Elkins and Wegner [4] discussed the problem of spasticity in paraplegia and mentioned the use of subarachnoid alcohol block, but stated that they had had no experience with that treatment. They advocated anterior rhizotomy, obturator nerve resection, and measures of that sort. They also discussed the use of curare, as well as skin and skeletal traction. Guttman and associates [5] stated that the injection of 1 to 2 cc. of 80% alcohol into the substance of the spinal cord temporarily relieved violent flexor spasms in three cases. Freeman and Heimburger [6] condemned the use of alcohol for relief of spasticity. However, they described a technique in which 0.5 cc. of alcohol is given into the spinal cord at each of three levels above the lesion. Two cubic centimeters was also injected into the spinal subarachnoid space with the patient on one side, and the procedure was repeated 10 days later with the patient on the other side. The authors reported that relief lasted from two days to six weeks. In another article,[7] Freeman and Heimburger described the same tech-

4. Elkins, C. W., and Wegner, W. R.: Newer Concepts in the Treatment of the Paralyzed Patient Due to War-Time Injuries of the Spine: Neurosurgical Complications, Tr. South. S. A. (1945) **57**:36 (Dec.) 1946; Neurosurgical Complications, Ann. Surg. **123**:516 (April) 1946.

5. Guttmann, L.; Riches, E. W.; Whitteridge, D., and Jonason, P. H. A.: Discussion on the Treatment and Prognosis of Traumatic Paraplegia, Proc. Roy. Soc. Med. **40**:219 (March) 1947.

6. Freeman, L. W., and Heimburger, R. F.: Surgical Relief of Spasticity in Paraplegic Patients: I. Anterior Rhizotomy, J. Neurosurg. **4**:435 (Sept.) 1947.

7. Freeman, L. W., and Heimburger, R. F.: Surgical Relief of Spasticity in Paraplegic Patients: II. Peripheral Nerve Section; Posterior Rhizotomy and Other Procedures, J. Neurosurg. **5**:556 (Nov.) 1948.

nique of injecting small amounts of alcohol and condemned the procedure. Freeman,[8] in articles published in 1949, again mentioned intrathecal injection of alcohol but condemned the procedure. Campbell and Whitfield,[9] in discussing the intrathecal injection of 1 to 2 cc. of alcohol for relief of pain as used by Dogliotti, with the patient in various positions, referred to a similar use of alcohol for the relief of spasticity. However, they did not cite cases. Bors and his co-workers[10] reported the use of alcohol intrathecally and other measures in the treatment of cord bladder. Their intrathecal injection of alcohol was usually given at the first-second lumbar interspace but was sometimes done as high as the eighth thoracic level. As a rule they used 10 cc. or more. The patient was placed in the extreme Trendelenburg position for 24 hours, and bed rest was advised for 6 days. A strict regimen of tidal drainage was used after the block was made. Thirty-five cases were reported on. In 10 of these the bladder capacity was below 200 cc. In 7 of these 10 cases the result was "good," and in 3 "poor." The authors stated that reflex contractions were absent after the block but that they tended to reappear at varying intervals. These intervals were as short as 1 month and as long as 21 months. The authors were of the opinion that a well-balanced bladder prior to block contraindicated the procedure.

PRESENT STUDY

Material and Method.—In my material, 12 patients with severe spasticity due to paraplegia were treated with intrathecal injections of alcohol. The study was begun at the suggestion of Dr. Thomas I. Hoen. There were 11 men and 1 woman. One of the men was quadriplegic. A total of 17 separate alcohol blocks were done. Three patients required repeated injections, and one patient required two additional injections. In every case the second or third injection was done simply for mild, but persistent, abdominal spasm. It was clear to the observer that the degree of this spasm was slight to moderate, but the patient was more upset by the residual spasm than was actually warranted. Nevertheless, to obtain a more satisfactory result, the injections were remade, sometimes at a higher level. In each case in which a repeated injection was necessary there was no spasm whatever in the legs or feet. In four patients a fracture dislocation of the spine was the cause of the paraplegia. Two of these lesions were in the cervical region and two were in the thoracic region. Three patients had shrapnel or gunshot wounds, all of which were in the thoracic region. Three patients had intraspinal tumors. Two of these tumors were malignant extradural neoplasms, and one was an intramedullary glioma. All were located in the thoracic region. One patient had had a fracture of the thoracic portion of the spine, and one had severe arachnoiditis. It is noteworthy that only three patients had wounds that were directly incurred as the result of battle action. All the others had injuries or disease which either did, in fact, occur in civilian life or could as well have done so. The time interval between the onset of the injury or disease and the injection of the alcohol varied from nine months to six years. In every case the spasticity came on within a few months of the time of injury or disease. The patient who received the alcohol block after only nine months had a histologically verified sarcoma.

The following technique of injection was used: The patient was placed on his side on a Stryker frame in the usual position for lumbar puncture. The mattresses of the frame were so arranged that a space was left in the lumbar region. An 18-gauge spinal needle was inserted

8. Freeman, L. W.: Treatment of Paraplegia Resulting from Trauma to the Spinal Cord, J. A. M. A. **140**:949 (July 16) 1949; 1015 (July 23) 1949.

9. Campbell, E., and Whitfield, R. D.: Symposium on Surgical Emergencies: Surgical Treatment of Intractable Pain, S. Clin. North America **30**:349 (April) 1950.

10. Bors, E.; Comarr, A. E., and Moulton, S. H.: Role of Nerve Blocks in Management of Traumatic Cord Bladders: Spinal Anesthesia, Subarachnoid Alcohol Injections, Pudendal Nerve Anesthesia and Vesical Neck Anesthesia, J. Urol. **63**:653 (April) 1950.

at the second-third lumbar interspace, with the beveled end pointing caudally. For repeat injections the needle was inserted at a higher level, usually at about the ninth thoracic. Ten cubic centimeters of spinal fluid was removed. With the help of assistants the patient was then turned into the supine position and the needle allowed to project downward through the already prepared space between the mattresses. The foot of the Stryker frame was next elevated so that the patient's body made an angle of about 45 degrees with the floor. A syringe containing 15 cc. of absolute alcohol was then attached to the needle via a short length of rubber tubing. The patient was asked to report any symptoms, such as paresthesias, giving both the type and the location. The alcohol was injected slowly while the patient's reaction was watched. As a rule, 30 to 60 seconds was required to complete the injection. Repeat injections amounted to as much as 20 or 30 cc. After the injection, the patient's legs were straightened out, and he was left in the position described for about one hour. At the end of that time he was transferred to his bed. At that time the bed was flat, or, if desired, the Trendelenburg position might be maintained for another few hours. Most patients were up in their wheel chairs the following day.

Results.—With regard to spasticity, the results have been excellent in all cases. In every patient spasticity and superimposed spasms were severe prior to the block. There was immediate and complete relief of spasticity and spasms in the legs in all patients. As mentioned previously, there was residual spasticity of a mild to moderate degree in the abdominal musculature of four patients. Although this led to reinjections in these patients, further experience indicated that such repeated procedures should be withheld unless the degree of spasm is severe. Other investigators have noted what they consider to be increased spasm above the level of the block as a late sequela. This has not occurred in my experience. The preblock treatment of spasticity included oral use of mephenesin, "depropanex" (deproteinated pancreatic extract), curare, and neostigmine; physical therapy, including galvanic stimulation; tenotomy, and obturator nerve sections. None of these measures gave any significant relief. Obturator nerve sections temporarily relieved the adductor spasms, but only partially. I believe that such resection has a place in cases of severe adductor spasm, sufficient to interfere with ambulation. This is especially true when residual spasm in other muscle groups, such as the quadriceps femoris, serves a useful purpose in maintaining stance during ambulation. Physical therapy sometimes reduced the superimposed spasms, probably as a result of fatigue, and had a beneficial psychological effect. There was no objective evidence, however, of reduction in spasticity. The maximum follow-up period was 20 months. During this time there was no return of spasticity in any of the patients.

Voluntary motion was absent in every patient before the block except in two, who retained a slight degree of movement at the toes. This movement was not of functional value. After the block none of the patients had any voluntary motion. All patients had hyperactive reflexes and pathological plantar reflexes before the block. In every patient reflexes were absent after alcohol injection. Before the block contractures were severe in five patients and moderate in the remaining nine. After the block contractures were overcome in every patient, in all but one completely. In the one remaining patient the contractures were nearly overcome, but the knees could not be straightened out to 180 degrees. Physical therapy was very useful in overcoming these contractures following the block. As a rule, patients with persistent partial contractures immediately after the block required from a few days to a week or two of daily physical therapy to straighten the legs. Before the block all sensory modalities below the level of the initial lesion were absent in all patients but one, in whom deep sensation was preserved. After the block deep sensation was

similarly preserved in this patient. Two patients had severe pain in the lower limbs before the block. Neither had relief from this pain. A third patient suffered from cramps in the legs before the block. After the injection of alcohol he complained of a squeezing sensation and electric shocks in his legs. He thought that these were worse than his previous cramps. This patient was one of those with a malignant extradural tumor. A fourth patient had severe pain in the legs for several days after the block. He also suffered from headaches, vomiting, and fever for a week after the injection. The degree of atrophy in the legs was not measured in these patients, but on inspection it seemed to be about the same in all.

All patients had constipation and required enemas both before and after the alcohol injection. Seven patients who carried catheters because of urinary retention continued to use their catheters after the injection. Two similar patients were able to discard their catheters, but one had a fairly large residual. The condition of retention in one patient with a suprapubic catheter was the same after the injection, and that of one patient with urinary incontinence was unchanged. One patient who did not need a catheter before the block did not require it after the block, but he had to strain to void. Nine patients had no bladder sensation, either before or after the block. Two patients had experienced abdominal fullness when their bladders were distended, but after the block this feeling was gone. One patient seemed to have sensation both before and after the block.

Cystometrograms were made in nearly every case both before and after subarachnoid alcohol injection. Three patients had normal cystometrograms after the block. Two of these had had cystometrograms made before injection, and both were normal. The third patient did not have a preblock cystometrogram. Five patients with hypertonic bladders before the block had a mild or moderate degree of hypotonicity of the bladder after the block. One patient with a hypertonic bladder did not have a postblock cystometrogram because of a severe febrile reaction which followed his initial test. One patient with a hypotonic bladder before the alcohol injection had a hypertonic bladder after the block. Another patient with a hypotonic bladder before injection did not have a cystometrogram afterward. In summary, it may be said that patients with normal cystometrograms before block did not undergo a significant change in their readings after the block. Patients with hypertonic bladders had improvement in the direction of hypotonicity. None of the bladders became atonic as the result of the block.

Data concerning sexual function were obtained for seven patients. All these had sensationless erections associated with spasms before the block, and in every case these were absent after the injection. Most of the patients stated that desire, fantasy, and dreams were about the same before and after the block. Genital sensation was absent in all patients before injection.

Decubitus ulcers were frequent and severe both before and after alcohol injection in all but one patient. In one patient four decubitus ulcers cleared up after the block with continuation of the surgical and medical management given before block. This strange result in all but one patient is contrary to the general impression entertained by most workers in this field. From these cases it seems clear that there was no actual change in the status of decubitus ulcers as the result of alcohol block. However, there is no question that the handling of the patient and the care of the ulcers in the ward are much easier when the patient is flaccid rather than spastic.

In addition, after surgical measures for the treatment of decubitus ulcers there seems to be less likelihood of friction resulting from spasms. It is not unlikely that a larger series of cases with carefully controlled treatment before and after block may show that there is, in fact, a beneficial effect upon the decubitus ulcers as the result of alcohol injection.

In my cases ambulation was changed only in that handling in a wheel chair was easier after the block than before. It may be that serious efforts to make the patient ambulant in braces would be easier as a result of the flaccidity which is produced, but my patients largely felt that they would prefer a wheel chair existence to the strenuous exertions of ambulation in braces. Ambulation was, of course, used for daily physical therapy, but no attempt was made to change the patient's basic method of locomotion after flaccidity was obtained.

The patient's subjective evaluation was recorded in every case. Each patient expressed himself as satisfied with what the alcohol injection had done for the relief of spasticity in his legs. Patients with continued spasms in the abdomen expressed dissatisfaction with that feature, but it did not seem to be of very great importance. The toxic effects of alcohol injection into the subarachnoid space were very slight or absent. One patient had pains in the legs, together with headache, vomiting, and fever, for four or five days. These symptoms then subsided. Another patient stated that he experienced transitory numbness, paresthesias, and weakness, extending up as high as the cervical region, within a few moments of the alcohol injection. These symptoms never became alarming and subsided within about 15 minutes. It is noteworthy that this patient was the second to receive the injection. The technique which was used in this case was not the one described above. With the first two patients I followed the technique of injection which had been described previously. This consisted of making the injection while the patient was lying on his side in the usual position for lumbar puncture. As soon as the injection was completed, the needle was withdrawn and the patient was turned on to his back. His head was immediately lowered. Attendant upon this procedure was a good deal of straining on the part of the patient. Undoubtedly, a small amount of the alcohol was forced upward in the spinal canal, instead of downward toward the sacral sac. It was precisely for this reason that the technique was changed, so that the injection was given with the patient supine and his hips already elevated. In every case an effort was made to get the patient to relax, and he was specifically told not to strain. The result was that the injection could be given in a more leisurely fashion; and if an amount insufficient to produce the desired result was at first injected, an additional quantity could then be given without changing the position of the patient or the needle.

COMMENT

The indications for subarachnoid injection of alcohol for the relief of spasticity are clear. Three basic conditions must be fulfilled before the patient is a candidate for intrathecal administration of alcohol: 1. The spasticity and spasms must be severe enough to interfere with both the comfort and the care of the patient. 2. There must be no residual motor function. 3. The lesion must be stationary.

The severity of the spasticity must be judged individually for each patient, and this judgment will, of course, depend greatly upon the observer and to a certain extent upon the patient. Most patients requiring injection of alcohol for relief of

spasticity will have either no motion in the lower limbs or, at best, only slight motion, which will be of no functional significance. Patients with malignant lesions of the spine or injuries of the spinal cord which are complete and which have been verified by operation will present no difficulty. Patients with clinically complete but surgically unverified lesions of the cord can usually be considered suitable after the lapse of one year. There must be no possibility of significant improvement in neurological function. Results in these cases also indicate that the bladder is not inevitably made worse. On the contrary, a hypertonic bladder is usually benefited. A normal or a near-normal bladder is not necessarily harmed by the procedure. However, no promise can be given the patient with regard to improvement of the bladder, and, in particular, with regard to the discarding of the catheter. The high percentage of patients in the series of Bors and his co-workers [10] who were able to discard their retention catheters was not attained in my series. Preservation of sexual and reproductive function in paraplegia is rare. When it does occur, it is usually in a patient with an incomplete lesion. It may be considered a contraindication to the procedure. There are no other contraindications if the above criteria are fulfilled. One patient with an intramedullary glioma died 17 days after the alcohol injection. As far as could be determined clinically, his death could not definitely be related to the injection. The terminal episode consisted of dyspnea, cyanosis, and fever, which was attributed to pulmonary embolism from his decubitus ulcers. Unfortunately, autopsy was not permitted. It is possible, therefore, that an embolus arose from one of the leg veins and that the change from spasticity to flaccidity allowed for the development of phlebothrombosis. If this thesis is correct, vigorous physical therapy begun immediately after the alcohol block might be of importance in prevention.

From this study, and from other studies reported in the literature, the following conclusions concerning the intrathecal use of alcohol in the treatment of spasticity in paraplegia are warranted.

1. The procedure when properly performed is simple, safe, and effective.

2. The relief of spasticity is immediate, and the results, within the time limits of observation, which in this series was 20 months, seem to be permanent.

3. The procedure is indicated in patients with stationary lesions of the spinal cord which have deprived the subject of useful voluntary motion in the legs and have resulted in severe spasticity.

4. There are no serious contraindications to the procedure when these criteria are fulfilled.

SUMMARY

The problem of the treatment of spasticity by means of subarachnoid injections of alcohol is discussed and the literature cited. Twelve cases, representing a variety of lesions of the spinal cord, most of which were "civilian" in type, are reported. A modified technique of alcohol injection is described. Intrathecal injection of 15 cc. of alcohol into the lumbar sac has been found to give immediate and "permanent" relief of spasticity of the legs. Beneficial effects upon the bladder, ambulation, and the attitude of the patient are likewise described.

RELATION OF SOCIAL ATTAINMENT TO PSYCHOLOGICAL AND ADRENOCORTICAL REACTIONS TO STRESS

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THIS PAPER reports the findings of a pilot study in a research project investigating the relations of social behavior and adjustment to (*a*) the pituitary-adrenal responses and (*b*) the psychological (overt behavioral) responses to experimental stress situations. The research project is motivated by the fact that both disturbed adjustment patterns and altered pituitary-adrenal function are implicated in such syndromes as schizophrenia,[1] asthma,[2] and hypertension.[3] In the pilot study reported here we attempted to determine whether there are significant relations between measures of social attainment and the pituitary-adrenal and psychological responses to the "stress" of the Target Ball Frustration test.

METHOD AND MATERIAL

Measures of Social Attainment.—The subjects were divided into an upper and a lower group with respect to education, occupation, formal group association, and over-all social attainment, as follows:

1. Education: Upper status required some schooling at the high-school level; lower status was assigned to subjects with only grade-school education.

2. Occupation: Upper status was assigned to skilled factory workers,[4] foremen, and supervisors; lower status, to semiskilled or unskilled factory workers, laborers, and nonofficer municipal firemen.

From the Worcester Foundation for Experimental Biology, the National Institute of Mental Health Cooperative Research Station at the Worcester Foundation, Public Health Service, Federal Security Agency, and the Worcester State Hospital.

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3. Perera, G. A.: The Adrenal Cortex and Hypertension, Bull. New York Acad. Med. **26**:75, 1950. Weiss, E.: Emotional Problems of High Blood Pressure, Am. J. Psychiat. **107**:264, 1950.

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3. Formal Group Associations: Upper status was assigned to officers of any formal groups and to participant members of community service organizations and semiselective social organizations, such as the Masons, Eagles, or Elks; lower status was assigned to nonofficer members of minimally or nonselective, lower-prestige social groups,[5] such as the American Legion, and to subjects with no formal group membership. Subjects belonging to both upper and lower groups were assigned upper status.

4. Over-All Social Attainment: Upper status was assigned to subjects with upper status in at least two of the three foregoing groups; lower status was assigned to those with upper status in at most one of the above.

Target Ball Frustration Test.—A simple pinball-like device, the Rotter aspiration board,[6] is manipulated by the experimenter so that the subject becomes inept after a period of successful performance. A level of aspiration technique is used; the subject states the score he thinks he will make (his goal) before each trial. The procedure and rationale of the Target Ball Frustration test are discussed in detail by Berkeley,[7] who collected the target ball test data used in this study.

TABLE 1.—*Increase in Rate of Excretion of 17-Ketosteroids Following the Target Ball Frustration Test (17-Ketosteroids Stress Score) for Each Subject and His Educational, Occupational, Formal Group Association, and Over-All Social Attainment*

17-Ketosteroids Stress Score	Education	Occupation	Association	Over-All Social Attainment
469	Lower	Lower	Lower	Lower
270	Lower	Upper	Lower	Lower
190	Lower	Lower	Lower	Lower
157	Upper	Upper	Upper	Upper
123	Lower	Lower	Lower	Lower
84	Upper	Lower	Lower	Lower
68	Upper	Lower	Lower	Lower
56	Upper	Lower	Upper	Upper
41	Upper	Lower	Lower	Lower
26	Lower	Lower	Upper	Lower
5	Lower	Upper	Upper	Upper
4	Upper	Upper	Lower	Upper
— 4	Lower	Lower	Lower	Lower
— 12	Lower	Lower	Upper	Lower
— 15	Upper	Lower	Upper	Upper
— 39	Lower	Lower	Lower	Lower
— 51	Lower	Upper	Upper	Upper
— 57	Upper	Lower	Upper	Upper
— 65	Upper	Upper	Upper	Upper
— 81	Upper	Upper	Upper	Upper
— 81	Upper	Lower	Upper	Upper

(*a*) The measure of pituitary-adrenal responsivity to the stress of the Target Ball Frustration test used in this study is the 17-ketosteroid stress score. This is defined as the increase in the rate of excretion in the urine of 17-ketosteroids in the stress sample (taken 15 minutes after the completion of the test) over the pre-stress sample (taken immediately before its inception). The biochemical determinations were made by personnel members of the Worcester Foundation for Experimental Biology. The procedure and laboratory techniques are given in detail by Pincus and Hoagland.[1a]

5. Hull, S. F.: Social Stratification in Worcester, Massachusetts, Thesis, Clark University, 1950.

6. Rotter, J. B., and Rodnick, E. H.: A Study of the Reactions to Experimentally Induced Frustration, Psychol. Bull. **34**:577, 1940.

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TABLE 2.—*Shift Scores in Target Ball Frustration Test for Each Subject and His Educational, Occupational, Formal Group Association, and Over-All Social Attainment*

	Status Scores			
Shift Score	Education	Occupation	Association	Over-All Social Attainment
2	Upper	Lower	Lower	Lower
3	Lower	Lower	Lower	Lower
6	Lower	Lower	Lower	Lower
9	Lower	Upper	Lower	Lower
9	Upper	Upper	Upper	Upper
16	Upper	Upper	Lower	Upper
25	Lower	Lower	Lower	Lower
28	Upper	Lower	Lower	Lower
29	Upper	Lower	Upper	Upper
30	Lower	Lower	Lower	Lower
30	Upper	Lower	Upper	Upper
32	Lower	Upper	Upper	Upper
33	Upper	Lower	Lower	Lower
38	Lower	Lower	Lower	Lower
40	Upper	Lower	Upper	Upper
42	Lower	Lower	Lower	Lower
43	Upper	Upper	Upper	Upper
45	Lower	Upper	Upper	Upper
48	Upper	Lower	Upper	Upper
58	Lower	Lower	Upper	Lower
70	Upper	Upper	Upper	Upper

TABLE 3.—*The 17-Ketosteroids Stress Scores Following Target Ball Frustration Test of Subjects with Lower Status (n) in Formal Group Associations Compared with Those of Subjects with Upper Status (m) in Formal Group Associations*

17-Ketosteroids Stress Scores		
Subjects with Lower Status		Subjects with Upper Status
n = 10	*U* * Values	m = 11
469	11	157
270	11	56
190	11	26
123	10	5
84	10	— 12
68	10	— 15
41	9	— 51
4	7	— 57
— 4	7	— 65
— 39	5	— 81
U obtained = 91		— 81

$$U \text{ estimated} = \frac{nm}{2} = 55$$

$$\frac{x}{\sigma} = \frac{U \text{ obtained} - U \text{ estimated}}{\sqrt{\frac{nm\ (n + m + 1)}{12}}} = \frac{91 - 55}{\sqrt{\frac{110\ (22)}{12}}}$$

$$\frac{x}{\sigma} = 2.54;\ p = 0.01$$

* This column indicates how many of the scores of the m subjects are exceeded by each score of the n subjects; e. g., 469, which is the highest score of the n subjects exceeds all 11 of the m subjects' scores.

(*b*) The measure of overt behavioral response to the stress of failing performance used here is the shift score. This is defined as the sum of the differences between the goals which were expressed before each of 15 failure trials and the mean of the goals which were expressed before the preceding 10 success trials. The shift score indicates the extent to which the subject lowers his goals after failure.

Design of the Study.—Twenty-one normal, nonprofessional men, ranging in age from 35 to 60, with a mean age of 46, were used. The scores of the subjects with upper status were compared with the scores of subjects with lower status. Eight comparisons were made.

(*a*) The 17-ketosteroid stress scores of subjects in the upper status group were compared with those of subjects in the lower status group in respect to (1) education, (2) occupation, (3) formal group association, and (4) over-all social attainment.

(*b*) The shift scores of subjects in the upper status group were compared with those of subjects in the lower status group in respect to (1) education, (2) occupation, (3) formal group association, and (4) over-all social attainment.

The probability that the scores of one group of subjects were larger than the scores of the other group due to chance alone was determined by using the *U* technique, a nonparametric, rank-order statistic.[8]

RESULTS

The data are presented in Tables 1 and 2. Table 3 illustrates the use of the *U* technique; the 17-ketosteroid stress scores of subjects with lower status in formal group associations are compared with the 17-ketosteroid stress scores of subjects with upper status.

(*a*) The ranked 17-ketosteroid stress scores are as follows:

1. The stress scores of subjects with lower status in education are higher than those of subjects with upper status in education but not at a statistically significant level.

2. The stress scores of subjects with lower status in occupation are higher than those of subjects with upper status but not at a statistically significant level.

3. The stress scores of subjects with lower status in formal group associations are higher than those of subjects with upper status at a statistically significant level ($p = 0.01$).

4. The stress scores of subjects with lower status in over-all total social attainment are higher than those of subjects with upper status at a statistically significant level ($p = < 0.03$).

(*b*) The ranked shift scores are as follows:

1. The shift scores of subjects with upper status in education are higher than those of subjects with lower status but not at a statistically significant level.

2. The shift scores of subjects with upper status in occupation are higher than those of subjects with lower status but not at a statistically significant level.

3. The shift scores of subjects with upper status in formal group associations are higher than those of subjects with lower status at a statistically significant level ($p = < 0.02$).

4. The shift scores of subjects with upper status on over-all social attainment are higher than those of subjects with lower status at a level tending toward statistical significance ($p = < 0.10$).

8. Mann and Whitney: On a Test of Whether One or Another of Two Random Variables is Stochastically Larger Than the Other, Ann. Math. Statist. **18**:50, 1947. Moses: Non-Parametric Statistics for Psychological Research, Psychol. Bull. **49**:122, 1952.

The probability that three of eight exploratory comparisons should exceed the 0.05 level of confidence by chance is less than 1 in 100.[9]

COMMENT

These findings may be briefly interpreted as follows:

Subjects with higher social attainment, particularly in the area of formal group associations, showed more adaptive responses to the Target Ball Frustration test. They were less stressed physiologically; i. e., less pituitary-adrenal response, measured by the increase in the rate of excretion of 17-ketosteroids, was evoked. They shifted their goals more realistically after failure.

In the continuation of this study, scales of social attainment and adjustment will be constructed, using material from psychiatric interviews with normal men. With the use of these scales, the subject's interpersonal adjustive mechanisms and his pituitary-adrenal and psychologic responses to experimental stresses will be explored further.

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PERSONALITY FACTORS IN DENIAL OF ILLNESS

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THE EXPLICIT verbal denial of illness or physical incapacity is not uncommon among patients with brain disease.[1] A person not only may disclaim hemiplegia or blindness but may deny that he is ill in any way, attribute his hospitalization to some minor symptom, or state that his incapacity is due to some trivial cause, such as "laziness." In a study of 22 people with brain tumors,[1a] it was found not only that such disabilities as hemiplegia and blindness were explicitly denied, but that the patients also denied the existence of traumatic experiences, such as a craniotomy, such symptoms as sphincteric incontinence, evident pain, and vomiting, and certain felt inadequacies in their life situation. These phenomena could not be explained on the basis of any unitary defect caused by a lesion in any particular area of the brain. It was, rather, that brain disease had produced a reorganization of function in which the patient denied anything that he felt was seriously wrong with him. The phenomenon of denial occurred never as an isolated manifestation but always as part of a more general alteration in behavior. This always included disorientation for time or place and usually language changes of a "paraphasic" type,[2] confabulations, changes in mood, and often reduplicative phenomena.[3] In all cases a bilaterally slow-wave electroencephalographic record was obtained. The lesions were deep-seated, usually infiltrating, and in most instances associated with increased intracranial pressure or subarachnoid bleeding.

However, in many cases in which these types of lesions and electroencephalographic records occur, explicit verbal denial of illness is not expressed. This difference, again, cannot be explained on the basis of anatomical localization or the severity of the pathological process, even though for the production of the syndrome

This study was aided by the Neurological Research Fund.

From the Neurological Service of the Mount Sinai Hospital, New York, and the Division of Neuropsychiatry, Army Medical Service Graduate School, Washington, D. C.

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3. Weinstein, E. A.; Kahn, R. L., and Sugarman, L. A.: Phenomenon of Reduplication, A. M. A. Arch. Neurol. & Psychiat. **67**:808-814 (June) 1952.

of denial an altered milieu of brain function is necessary. Thus, one patient with a tumor of the third ventricle may deny visual loss and sexual impotence, while another may become disoriented and paraphasic but will admit all his disabilities.

A number of authors have indicated the importance of preexisting personality factors in the development of the delusion of denial. Sandifer,[4] in cases of anosognosia for hemiplegia, stressed motivational factors. He interpreted the denial of paralysis in terms of Goldstein's concept of the avoidance of the catastrophic reaction. Wortis and Dattner,[5] describing a case of denial of left hemiplegia, considered the matter of the patient's reaction to illness. Williams and Rupp,[6] in a study of patients with confabulation, which included many with denial, characterized them as having been introverted, incapable of observing themselves objectively, and with a tendency to self-deception. These authors noted that, in sharp contrast to hypochondrial patients, patients with confabulation seemed to have had no concern with their bodies. Goldstein [7] stated that denial is in itself not a pathological manifestation but is present to some degree in all persons. Weinstein and Kahn [10] also stressed that the brain lesion did not cause the denial but created the conditions of perceptual symbolic function in which it appeared in delusional form. They noted that the most complete and persistent denial occurred in compulsive, perfectionistic persons.

The present study is an attempt to evaluate systemically the role of personality factors in the behavior of patients with denial of illness by comparing the backgrounds of patients with explicit verbal denial with that of patients who do not verbalize denial under similar conditions of altered brain function.

MATERIAL AND METHODS

Twenty-eight patients who expressed a consistent explicit verbal denial of one or more major aspects of illness were studied. These patients denied their disabilities on direct questioning for at least one week. Of these, 11 denied left hemiplegia; 6 denied a pronounced visual defect; 18 who were confined to bed denied being ill in any way or attributed hospitalization to some trivial cause, and 14 denied that a craniotomy had been performed. Seven patients who were incontinent of urine denied it, and two patients with a history of sexual impotence denied it.

The diagnostic categories are tabulated as follows:

Gliogenous frontoparietotemporal tumor	8
Diencephalic tumor	4
Metastatic brain tumor	2
Acoustic neurinoma	2
Pituitary adenoma	1
Subfrontal meningioma	1
Cerebrovascular disease	5
Aneurysm of the circle of Willis	4
Vascular anomaly of right parietal lobe	1
	28

4. Sandifer, P. H.: Anosognosia and Disorders of Body Scheme, Brain **69**:122-137 (June) 1946.

5. Wortis, H., and Dattner, B.: Analysis of a Somatic Delusion: A Case Report, Psychosom. Med. **4**:319-323 (July) 1942.

6. Williams, H. W., and Rupp, C.: Observations on Confabulation, Am. J. Psychiat. **95**:395-405 (Sept.) 1938.

7. Goldstein, K.: The Organism: A Holistic Approach to Biology Derived from Pathological Data on Man, New York, American Book Company, 1939.

All these patients had electroencephalographic records showing bilaterally abnormal slow-wave activity, of frequencies ranging from 1 to 6 cps. All the patients showed alterations in behavior, including disorientation for place and time (28 patients), alterations in language of "paraphasic" type (19 patients), and sphincteric incontinence (22 patients).

A group of 28 patients with comparable lesions, similar electroencephalographic records, and alterations in behavior which did not include explicit verbal denial of illness were also studied. All these patients also showed disorientation for time and place; 23 had "paraphasic" language, and 23 were incontinent of urine. Of this group, all had obvious incapacity; 15 were hemiplegic; 4 had pronounced visual defects, and 11 had had craniotomies. Two patients had a history of sexual impotence. None of these defects was denied, and all patients admitted being ill.

The diagnostic categories in the group without explicit verbal denial were as follows:

Gliogenous frontoparietotemporal tumor	8
Diencephalic tumor	4
Metastatic brain tumor	4
Pontine tumor	1
Cerebrovascular disease	4
Aneurysms of the circle of Willis	4
Olfactory-groove meningioma	1
Subfrontal meningioma	1
Pituitary granuloma	1
	28

The clinical diagnoses were verified at autopsy (14 patients), craniotomy (32 patients), and on clinical and roentgenographic evidence (10 patients). Four patients with the kind of electroencephalographic changes described were too drowsy to permit proper evaluation of their status and were not included in the series. Eight patients who showed inconstant verbal denial were also omitted.

Data on the premorbid personality were obtained in interviews with relatives, friends, employers, and employees. The informants were asked to describe the patient as they had known him previously and to cite the changes that they had noted since the onset of his illness. A check sheet concerning the following was used.

1. Attitudes: Those toward health and illness, food, work, money and property, sex, cleanliness, neatness, punctuality, and ethical concepts, such as duty, religion, honesty, and right and wrong.

2. Character of drive: Creativeness; imaginativeness; competitiveness; compulsiveness; need for superiority; prestige values; reaction to failure.

3. Reaction to stress: Temper outbursts; euphoria; humor; depression; indifference; sleepiness; worry; overt anxiety; physical symptoms; use of alcohol.

4. Interpersonal patterns: Degree of maturity; capacity for love and interchange of feelings; dependence; passivity; self-sacrifice; domination; manipulation; stubbornness; need to be right; pedanticism; practicality; suspiciousness; jealousy; tolerance; sensitivity; adaptability; self-consciousness.

Use of symbols: Sayings; superstitions; resolutions; promises; clichés; confabulations; prayers; profanity; manner of speech; gestures; mannerisms; habits.

RESULTS

Observations of Behavior in Patients with Explicit Verbal Denial.—Most of the patients with complete denial were bland and affable and had an air of unconcern. During interviews they answered questions readily and did not become agitated even by direct and repeated questioning about their defects. There were reduced spontaneous conversation and ideation, and speech contained many clichés and banalities. From the standpoint of hospital administration these patients were well behaved. They did not complain about their major symptoms and accepted

medication readily. Almost all were incontinent of urine but did not complain or seemed unaware of lying in a wet bed. Transient paranoid reactions occurred in eight patients.

Six other patients in the group showed a predominantly paranoid motivation, as illustrated in Case 2. In them the denial was not as complete. One patient with a tumor of the right temporal lobe denied that she had a hemiplegia or had had an operation but charged that the hospital had given her a cancer. She admitted being too weak to walk and attributed this to inadequate diet. Another woman said she could not move her hemiplegic side because it was sore from injections. These patients were more restless and complaining. They would ask repeatedly to be allowed to go to the bathroom to move their bowels. They complained about the meals and medication and in three instances expressed the delusion that the food was poisoned. They protested that the nurses were not caring for them properly. Five showed unusual sexual behavior, consisting of exposure, masturbation, sexual advances, or delusions that sexual advances had been made to them.

In expressing denial, the patients seemed to regard themselves or their physical defects as something outside of them. They sometimes referred to themselves in the third person, as "He didn't have an operation" or "She feels very well today." They commonly talked about the paralyzed limb as "he," "she," or "it." Thus, the patient described in Case 1 called her arm a "dummy." Another woman said the paralyzed limb was her "little daughter." A man referred to his arm as "an old piece of equipment that doesn't work." Patients commonly stated that the paralyzed limb was not theirs but belonged to someone else. One woman thought that an "extra" or a "false" limb had been placed in her bed. A patient in whom left hemiplegia developed during an arteriographic study immediately patted her left arm, remarking to the anxious physician, "There, there, don't worry; you'll be all right." Some patients, on encountering the useless limb, would fling it away from them. There was a good deal of emphasis on the proper words. One patient, although he complained of the "hammering and sawing" that had been done on his head, still did not say that he had had a craniotomy. Patients would state that "the arm is heavy" or "lazy" but would not admit that it was weak. The patient who charged the hospital had given her a cancer denied she had had a tumor or an operation. When in the course of recovery the denial was given up, such expressions as "I was *told* I had an operation," or "The *doctors* say I had a stroke, or "My legs, *they* don't move" were used.

Behavior in Patients Without Explicit Verbal Denial.—The group who expressed no verbal denial showed much more variability, both as between patient and patient and in the course of individual behavior. Twelve were noisy, demanding, and restless. They would shout for the nurses and express affection and resentment alternately in childish fashion. After calling for a urinal, they might urinate in bed or fill it and spill the contents. Sixteen patients exhibited abnormal sexual behavior, such as exposure. Seven made jests and puns; some were euphoric, while others were bitter and sardonic. Eleven were depressed and lethargic and slept a good deal. A patient with a tumor of the right thalamus showed successively different types of behavior over a four-month period. During the first week in the hospital she was euphoric and joked in sexual terms. She then became

querulous and demanding, accusing the nurses of neglecting her. After several weeks she was extremely depressed, talked very little except to her sister, and refused to eat. During this period she at no time denied that she had hemiplegia or had undergone an operation. In the course of a single day one patient was noted as euphoric by one examiner, paranoid by another, and depressed by a third.

PREMORBID PERSONALITY

Patients with Explicit Verbal Denial.—The patients with verbal denial had, in their interpersonal relations, placed a value on experiences that far transcended their utilitarian, material content. Their attitudes toward health and illness, work and leisure, and money and property had become more tied up with prestige and "security" than with enjoyment and actual utilization of these modalities for their intrinsic qualities. In the maintenance of this system a good deal of stress had been placed on verbal symbols. Words served a purpose far exceeding that of referential communication. The operation of this pattern was well illustrated in the accounts of the patients' attitude toward illness.

All these patients seemed to have always regarded illness as an imperfection or weakness or a disgrace. There was a strong trend to deny its existence. One patient with rheumatic heart disease insisted that her husband keep it a secret from the neighbors. Illness seemed to mean a loss of prestige in the eyes of others, and this had to be denied or justified. A number of patients would conceal their symptoms because they did not want to "worry" anyone. It had generally been difficult to get them to go to doctors, or even to stay home from work when they were ill. Relatives described these attitudes in such phrases as "always made light of things," "never complained," "fought against being sick," "never would go to a doctor or pamper himself," "wouldn't let himself get off his feet." The use of various resolutions, homilies, clichés, justifications, and rationalizations was frequently reported. "Once you admit you're sick, you are licked," "I've never had anything wrong before," "I'm sure I'll feel better tomorrow" are examples of the use of verbal symbols to solve the problems of illness. One patient consulted an ophthalmologist for blurring of vision early in her illness. He told her that she might have a brain tumor. She visited a number of physicians, who concurred in this opinion. She finally found a doctor who attributed her symptoms to the menopause. After this, despite a progressions in her symptoms, she refused to have any further medical help. Toward others who were ill these patients were generally very considerate and solicitous. Their advice was often reassuring. With one exception, they were regarded by the informants as strong, "independent" people who were able to shake off or ignore their own troubles and counsel others.

In their work the patients were described as having a great deal of drive and compulsive energy. Such expressions as "always on the go," "never could sit around," "never idle," "a human dynamo," "nothing too much for her as far as work was concerned" were used. One got the impression of a feeling of guilt or uneasiness if they were not occupied. They were invariably characterized as very conscientious, with a highly developed sense of duty and responsibility. It seems that work did not give a sense of satisfaction from a creative effort but was, rather, a means of attaining a position that would be above censure. Many seemed to feel

that any criticism was a destructive attack on their personal integrity. None was described as an original or imaginative person, and all were considered rather conventional.

The need for prestige and the esteem of others was a prominent motivation in all interpersonal situations. The word "pride" was almost invariably used by the patient's family. They would try to avoid, in a great majority of instances, being indebted to or accepting help from others. They were considered "reserved," rather than openly affectionate or emotional people. Almost all were respected, and in many cases they were the dominant member of the family group. They were people who were concerned with "principles" and "being right." All were described as being very honest and scrupulous.

Attitudes toward money and property were of interest. At first there did not seem to be any consistent pattern. Most were described as being thrifty; some were considered liberal with money; others were regarded as saving in some ways and extravagant in others. One man, for instance, was "stingy with his family" but would "throw money away on his friends." What was consistent was that money was not regarded primarily for the intrinsic satisfaction that it could bring but seemed to be used as a symbol of personal integrity. Thus, the patient who was stingy with his family felt that being generous here would make him seem weak while spending liberally on his friends would establish him as a successful man of the world. Several women spent large amounts on clothes when it involved factors of prestige. In others saving seemed to be a virtue in itself. A combination of these attitudes often seemed to result in a "penny-wise and pound-foolish" situation.

Some significant differences were noted between patients who expressed denial in a serene, affable fashion and those who showed predominantly paranoid behavior. Both had the same compulsive drive, the need to deny imperfections, the concern with prestige; but the paranoid group had expressed their needs and feelings in a more "physical" way. They were described as having violent tempers and having been irascible. They were restless physically; were "always moving on to another town," "could not stay in the house, always had to be going out." Their attitude toward illness was either open fearfulness or resentment. One could not go to doctors because he could not stand the sight of blood. Another had always expressed a hatred of doctors. The patient described in Case 2 had always admired doctors but was frightened of "needles." Another patient had formerly been hospitalized for an operation on a pilonidal cyst but fled before it could be performed. The use of "physical" symbols was also seen in the greater concern with personal appearance, bodily cleanliness and odors, bowel habits, and fussiness about food and diets shown by these predominantly paranoid patients. There was also great concern with the overt attributes of masculinity and femininity. The patient described in Case 2 was unhappy over his small stature and was ready to fight over any affront. Another patient would assert his authority in the family by whipping his son. A woman insisted that her husband kiss her on leaving for and returning from work. These patients showed marked overt sexual activity, five engaging in extramarital affairs. In the predominantly nonparanoid group little information about sexual attitudes was obtained, possibly in line with the general tendency to conceal feelings. It is significant that, while abnormal sexual behavior and verbal denial were not uncommonly associated, the most pronounced sexually aberrant

manifestations occurred in patients with little or no verbal denial. Two of the six paranoid patients had used alcohol more than moderately.

Patients Without Explicit Verbal Denial.—The accounts of the premorbid personality in this group were so varied that no single consistent pattern could be distinguished. These patients showed marked differences, however, from the patients who had explicit verbal denial of illness. None had shown previously the tendency to deny, ignore, or rationalize illness or incapacity. Illness was regarded as a problem in itself, not as a disgrace or an inadequacy. Those patients who were described as having been frightened of illness had gone to doctors willingly. Four were described as having been hypochondriacal, one man having been hospitalized for vague complaints on eight occasions.

Thirteen patients were described as having been hard, conscientious workers, but the aspects of competitiveness and prestige were less marked. There appeared to be less of the "ascetic spirit" and more capacity to enjoy things for their intrinsic values. The qualities of cleanliness and meticulousness occurred in each group with equal frequency. Five patients were regarded as imaginative and creative in their activities.

They were described as being more open with their feelings, more "emotional," and more capable of intimate interpersonal relationships. Ten were characterized as having explosive tempers. In contrast to the group with explicit verbal denial, 12 patients were characterized by relatives as being "dependent." This does not mean that these patients were necessarily more "dependent" in an absolute sense, but it indicates, rather, that their means of expression of their needs had been more overt, so as to be recognized by relatives. Likewise, the patients without explicit verbal denial had apparently been more open in the expression of their attitudes concerning sex. Thus, eight were quoted as having expressed strong dislikes for sexual intercourse.

None of the patients with verbal denial had had a psychotic episode. One patient in the group without verbal denial had a history suggestive of paranoid schizophrenia. He sustained a subarachnoid hemorrhage with weakness of the right side, which he admitted. Far from denying illness or operation, he charged that the electroencephalographic recording was an operation on his brain which would make him "crazy." Three of the patients in this group had been heavy users of alcohol.

REPORT OF CASES

The following cases are illustrative. For purposes of comparison, three patients with left hemiplegia are chosen.

CASE 1.—An unmarried woman aged 47, a factory worker, was admitted to the Mount Sinai Hospital on Aug. 18, 1949. Neurological examination showed complete paralysis of the right third cranial nerve and left hemiplegia. She denied she was ill or paralyzed, and she was disoriented for time and place. Lumbar puncture revealed xanthochromic spinal fluid, and the electroencephalogram showed diffuse 2-to-3 cps delta activity. Although she kept her right eyelids closed, she denied having double vision. She claimed that she was able to walk and that she could move her left limbs. She was incontinent of urine and would on occasion admit that she had wet her bed. She confabulated that she had recently been married. On Sept. 23 she touched her left arm and claimed that she felt it breathe, but then remarked, "He's only a dummy." On Sept. 25 she admitted that her left arm did not move but ascribed it to "laziness." Her manner with the staff was one of affable jocularity, with mild sexual connotations, address-

ing them by first names with easy familiarity. It was not until Sept. 26 that she admitted the weakness in the left limbs, and on that day was able to move her fingers slightly. She expressed the belief that the paralysis was due to pain and stiffness. On Oct. 20 the patient admitted for the first time that she kept her right eye closed because of double vision. Disorientation for time continued until Oct. 7; the electroencephalogram on Oct. 4 was normal. On Oct. 15 the patient was given 4½ grains (0.29 gm.) of amobarbital (amytal®) sodium intravenously and confabulated that she had walked home the previous evening. Actually, she was not able to walk without assistance until Nov. 16.

The following account of the patient's personality was obtained from her brother and sister-in-law. She was energetic, conscientious, and worrisome. She had worked for the same firm as a key groover for 30 years and was highly esteemed by her employers. "If she did something and it wasn't quite right, she would do it over and over again. She was never idle. In her spare time she would sew or wash or iron or come over to our place and rake leaves." She was conventional in her habits and was well liked in her community, being active in clubs and other social groups. She was devoutly religious and had a rigid moral code concerning honesty, duty, and respect for authority. Although sensitive to criticism, she was apt to be critical and bossy with others, liked to give advice, and was stubborn in getting her way. She was generous with people and often went out of her way for friends. While talkative and usually high-spirited, she would keep any troubles to herself and never wanted sympathy. She prided herself on being an "independent" person. Her health had been excellent, and her relatives had never known her to miss work. She had been constipated for many years but disliked going to doctors or taking medicines.

In most respects she was thrifty but would spend a good deal on clothes and give very generous presents. She was meticulous about her personal appearance, particularly about her hair. She got along well with groups of girls but was not an openly affectionate or demonstrative person. She was very particular about the men with whom she associated. She broke up with one boy because he wasn't intelligent enough and objected to another because his handkerchiefs were not clean. At the time of her illness she was engaged, but the marriage had been postponed several times.

During 1946 the patient had had several fainting spells, which she disregarded. In the summer of 1948 her relatives noted that her eyes were crossed. When it was brought to her attention, she would usually say, "You're crazy," or "There must be something the matter with your eyes." Her visual difficulties progressed, but, though she could no longer see television shows clearly and was obviously worried, she would not go to a doctor. In July, 1949, there developed weakness of her left limbs and an ataxic gait. At meals her left hand would drop into a dish, but she seemed to disregard it. Her only complaints were of gas pains and constipation. When she was finally persuaded to enter her local hospital, early in August, she was noted to be euphoric and incontinent of urine. She related that the Virgin Mary touched her arm and said, "You'll be okay." However, the patient still insisted to her relatives that she felt fine and that there was nothing wrong with her.

The patient showed complete denial of illness, refusing to admit her paralysis or diplopia. In her characterization of the paralyzed limb as a "dummy," the attitude toward the defect as something apart from the self is seen. The patient, in her confabulation of being married, also denied the problems of her relation with her fiancé, and, for the conventional person she was, the stigma of being unmarried. The stereotypy and conventionality are well illustrated in her report of the Virgin's remark, "You'll be okay." Her premorbid personality shows that throughout her life she had denied anything that might lead to a loss of esteem of others. She seemed to regard queries about her early symptoms as aspersions on herself.

CASE 2.—A man aged 46, a mechanic, was admitted to the Mount Sinai Hospital on July 10, 1950. Ten days previously he had complained of a sudden right-sided headache, after which marked weakness of his left limbs developed. He was seen by four doctors before he consented to be taken to a hospital near his home. There, lumbar puncture yielded bloody spinal fluid. After four days he had persuaded his wife to take him home.

Neurological examination showed paralysis of the upper left extremity and pronounced weakness of the left lower extremity. There were marked diminution of all sensory modalities over the left side and left homonymous hemianopsia. The deep reflexes were more active on the left, with a Babinski sign on that side. Lumbar puncture yielded xanthochromic fluid under normal pressure. The electroencephalogram showed diffuse slow waves of frequencies as low as 1.8 cps, with focal accentuation in the right frontal region.

On the day of admission the patient denied completely that there was anything wrong with his arms or legs. On the following day, when asked whether he could move his left arm, he said, "It doesn't function as I want it to, but there isn't anything wrong with it. If I could only go to the bathroom, I'd be all right." Two days later, when asked how his arm was, he replied, "Better." When asked then what was wrong with it, he said, "Nothing; it's just heavy." On July 17, seven days after admission, he remarked, "My left hand doesn't do what I want it to do, but there is nothing wrong with it." When asked why he came to the hospital, he answered, "For a rest, but I might have a blood clot on my brain." When asked whether he was worried about his condition, he replied, "No, it never happened to me before; so why should I worry now?" He had been incontinent of urine but denied it. The following day he admitted that his left extremities were "a little weak," but he thought that he could walk well. He remarked that his left arm and leg had previously been weak. He complained frequently of headache and constipation. He said that the headaches had come because the doctors had pounded his head. He blamed his condition on ill treatment received in the other hospital. He complained that another patient had stolen his toilet paper. He accused his wife of going out with one of the "good-looking doctors" and wanted her to remain with him all the time. He thought that a patient in a nearby bed had called him a "queer." The content of the patient's fears was brought out in his response to the "body symbol test." He was asked to give some common expressions using names of various parts of the body. He replied: "They are breaking my balls"; "Take an arm and a leg"; "They are leeches (the last apparently in reference to a contemplated arteriogram).

During his first 10 days in the hospital the patient was restless. He masturbated and exposed himself. He was disoriented for place, naming the hospital correctly but displacing it to an address one block from his home. He was incontinent of urine, sometimes admitting and sometimes denying the condition. He confabulated that during the war he had served in the infantry in France. He stated that he and his wife were each 36 years old, whereas he was actually 46 and his wife 31. He misidentified other patients, claiming that one was a prominent cafe-society figure and said that he had been visited by a movie star. He confabulated that both his parents were living.

On July 27, on the 14th day after admission, he admitted completely the weakness of his left limbs. At this time he was fully oriented for time and place. Despite the return on the same day of ability to move his left hand and fingers, he was very anxious. He would avoid answering questions about his condition. The only abnormality expressed was that he still thought that the patient in the next bed was a man who worked in his shop. The patient became so anxious and frightened that he left the hospital against advice, only to appear in the private office of one of us the next day in a state of panic.

After being at home for two weeks, he insisted on returning to work, but was not able to perform with his former efficiency and left after a month. During this period he drank a good deal. He described spells in this way, "If I walk along the street and see someone, I'll think I know him, but I just can't place him—I get all steamed up, dizzy, and nauseous, like I'm closing up in the chest—then I have to go in a different direction, for if I stay I'll pass out."

Subsequent examinations have shown persisting left homonymous hemianopsia and a slow-wave electroencephalographic region. The patient has been aware of the visual disturbance.

The patient was described by his wife and elder sister as an energetic, restless person who couldn't relax. He was extremely conscientious in his work, and eager to please his employer, and customers. He was perfectionistic, and no job was too hard for him. He resented anyone's thinking that a task was beyond him or that he was afraid of anything. He was very sensitive to any criticism and would not get over it for a long time. However, he would never show he was hurt or unhappy and was generally regarded as a jolly, carefree fellow. Only with his wife

at times could he ever let himself appear depressed. He was always an optimist. When any trouble came up, "he would put it out of his mind." A favorite expression was "If you think of the worst, it will happen to you."

The patient was very much concerned with prestige, particularly as it concerned "masculinity." He was self-conscious over his small stature (5 ft. 6 in., or 167.6 cm.) and his bad teeth. He would say, "If I were taller and had good teeth, I would own the world." Rather than let anyone think that he was afraid, he would offer to fight, but he generally controlled his temper. He was concerned with his sexual potency and had worried a great deal that his wife, who was 15 years his junior, might leave him for a younger man. If any one made a slighting remark, he would insist that they retract it or apologize.

The patient's health had been good. He had been bothered with constipation and headaches but had been too frightened to go to doctors. He was particularly fearful of "needles." If he felt ill, he would say that one had to fight such things off. With this, he had a great admiration for doctors, particularly women doctors. He had made friends with the interns in a hospital near his home and was thrilled at the opportunity of watching operations and autopsies. During the war he had driven an ambulance in his spare time. Several weeks prior to the onset of his acute illness he had been struck on the head by a 75-lb. (34-kg.), weight but, characteristically, had told his wife that he had scratched himself in his sleep. With other people who were ill or in trouble the patient was uncomfortable, but was described as being very generous, "He gave them the shirt off his back."

The patient had been somewhat preoccupied with bowel functions. If he did not have a movement every morning, he would become concerned and take laxatives or "roughage." He also was much concerned with personal cleanliness and odors and was meticulous about his appearance. He was not particularly fussy about food. He had been a fairly heavy drinker but had always worked regularly. Under the influence of liquor he would show some euphoria but would become very jealous of his wife.

The patient was the sixth child and second boy of eight children and had been considered a timid, obedient youngster. The informants believed that his mother had distinctly favored his elder brother, but the patient had always expressed great attachment to and admiration for his parents. He left school at the age of 14 to work and at 18 married a woman five years older than he who had had two illegitimate children. The marriage was an unhappy one, the wife giving him much personal abuse and expressing open contempt for him. He believed that the reason for the discord was that he had not satisfied her sexually. The marriage was terminated only on the woman's insistence. The patient had known his second wife for 10 years, and his present illness began three days after the marriage. During the period of the courtship the patient had been very jealous of his wife whereas he had had frequent relationships with other women. He had considered these "necessary" to preserve his health.

In this case the hemiplegia was denied, as the patient attributed his incapacity to sources outside himself. The proper words were important, as the patient stated that, while his arm did not move properly, there was nothing wrong with it. Like the other paranoid patients, he had been overtly concerned with his bowels and sexual potency. His aims in life seem to have been to appear powerful, happy, and popular, to satisfy women sexually, and to move his bowels regularly. With the improvement in brain function, he became oriented, and power in the left limbs returned. However, at the higher level of function the syndrome of denial could no longer be maintained, and severe anxiety developed, despite the patient's clinical improvement. This is analogous to the "withdrawal syndrome" which occurs with abrupt cessation of drugs in an addicted patient.

CASE 3.—A housewife aged 47 was admitted to the Mount Sinai Hospital on Oct. 20, 1949. Eight hours before admission she had sudden onset of left hemiplegia. There was a known history of rheumatic heart disease since the age of 12 years.

Examination on admission showed pronounced left hemiparesis. A left homonymous visual field defect could be demonstrated on gross confrontation. The patient tended to keep her head

and eyes rotated to the right, but no paralysis was present when she was asked to look to the left or on pursuit. There were astereognosis in the left hand and pronounced impairment of both position and vibration sensation in the fingers and toes on the left. There were rough systolic and diastolic apical murmurs. Lumbar puncture yielded a clear fluid under an initial pressure of 150 mm. of water. An electroencephalogram showed a diffuse amount of delta activity, with frequencies as low as 0.6 cps. The degree of abnormality was greatest at the right inferior frontal, inferior parietal, and ear-lobe electrodes.

On admission to the hospital, the patient was drowsy and restless, but after the first two or three days this condition alternated with a euphoric state. She appeared to neglect and be unaware of her left limbs. She was disoriented for time of day and partially disoriented for place. She did not deny her illness or paralysis verbally. When questioned about her disability, she would admit it in a punning, joking manner. This was also evident in her response to questions involving orientation, identification of people and objects, and other aspects of the examination. When asked whether there was anything the matter with her left arm, she stated, "Its slow on the uptake; it doesn't do what I want it to do—I need a new carburetor, I guess." When asked why she came to the hospital, she replied, "I was admitted at the whim of a doctor, but I think I have a clot somewhere." She remarked, "My left arm and leg don't synchronize—can you spell that?" When asked to identify one of the examiners, she quipped "Willie Wiseguy." She called the curtain rod by her bed a "trapeze." At times her mood and speech were manic, as "jokester-huh-prankster—did you ever see a hamster? It would take a lot of them to make a coat." She told humorous, off-color jokes to the doctors and nurses. She was incontinent of urine but did not deny it. When asked to draw a person, she omitted the limbs on the side which was the mirror image of her own left side.

Her euphoria, disorientation, and incontinence persisted until the last week in November. After this she appeared depressed, despite a beginning return of power in her left limbs. An electroencephalogram taken on Dec. 15 showed diffuse slow activity over the right side, with very little on the left.

A description of the patient's premorbid personality was obtained from her husband. She was considered a happy, openly affectionate person. Though possessed of energy, she was able to relax comfortably and did not resent the limitation of activity necessitated by her cardiac condition. Although not a complainer, she went willingly to doctors. Despite her husband's small income as a science instructor, she did not worry about money. She was not obsessive about details. She was a creative, imaginative person, interested in the small country house that the couple had bought and in making pottery and jewelry. Prior to her marriage she had been a school teacher. As an example of her imagination, the informant told a story of how she had reprimanded her pupils for failing to remove snow from their boots before entering the classroom. She remarked, "I just saw six Eskimoes in the coat room with melting snow dripping from them." She liked people, and was not self-conscious or greatly concerned with her pride or prestige. She had a temper, which she would use on occasion. She had always had a good sense of humor, and her husband remarked later that he was surprised not at the content of her jokes but that she told them to people that she did not know.

This patient did not explicitly deny her illness or hemiplegia. Indirectly, she expressed denial by averting her gaze from the paralyzed left limbs; graphically, in her representation of a human figure, and implicitly, by the use of the symbolic modality of humor. In contrast to the personality factors in Cases 2 and 3, her personality background did not show obsessive features, and verbal denial was not a habitual form of defense.

COMMENT

The term "explicit verbal denial" has been used in preference to "denial" or "anosognosia" because all the patients studied showed some form of denial of illness. Explicit verbal denial denotes the words "I am not sick" or "There is nothing the matter with my arm." It does not include the patients who, while admitting a paralysis, ignored the affected limbs and lay with their head and eyes deviated to

the opposite side, even though lateral head and eye movements could be performed on command and on pursuit. Such patients, when asked to draw a figure of a person, commonly expressed denial graphically by omitting the limbs on the figure on the side which was a mirror image of their own paralyzed limbs. The usual concept of anosognosia does not include patients who in response to questions about their illness become mute or appear to go to sleep. It likewise does not refer to patients who, while admitting a serious illness verbally, insist on getting out of bed to go out. All these aspects of behavior appear to be symbolic expressions of denial.

While for purposes of study they have been described separately, these modes of behavior are not individual defects caused by lesions of specifically different locations. They are manifestations of an alteration in brain function that is common to all types. Under these conditions patients with and without explicit verbal denial show the same patterns of disorientation,[8] paraphasia,[2] and reduplication.[3] While the patterns are constant, the elements vary, and these are in large part determined by the patient's own experience. In the cases described, it is evident that the denial did not appear suddenly with the onset of the brain lesion, but that it was a continuation of a preexisting personality trend. Brain disease does not cause denial. The tendency to denial is present to some extent in all people. The altered brain function creates a milieu in which new symbols for its expression can be evolved and maintained. The particular symbols used, when in the form of explicit verbal denial or such implicit forms as humor or muteness, motor overactivity or apparent sleep, appears to be mainly related to personality factors.

Many features of the personality pattern of patients with verbal denial have been noted by Sullivan [9] in his account of the obsessive person. Sullivan regarded the obsessive as using words in a magical way to overcome a lifelong state of profound insecurity. He described the omniscience and omnipotence in which the obsessional person maintains that he is right. One can tell him nothing, as he persists in denying the obviously unhappy situation in his life. He is ashamed of illness. He has the faculty of regarding himself as outside the self and, as it were, watching himself perform. In Sullivan's words, "They are always trying to make themselves do this or do that or be this or be that which is regarded as desirable." In telling an incident, he can overlook so many aspects as to present an account unrecognizable as the actual situation in order to fit his determination as to what the situation must be. All these features are seen in striking fashion in the patient with verbal denial, as with an air of serene equanimity or tragic persecution he maintains that he is perfectly well.

These observations are germane to some of the problems of prefrontal lobotomy. After lobotomy, patients show all the aspects of the syndrome of denial, i. e., disorientation,[10] confabulation, reduplication,[11] paraphasic language,[12] alterations in

8. Weinstein, E. A., and Kahn, R. L.: Patterns of Disorientation in Organic Brain Disease, J. Neuropath. & Clin. Neurol. **1**:214-226 (July) 1951.

9. Sullivan, H. S.: Conceptions of Modern Psychiatry: The First William Alanson White Memorial Lecture, Washington, The William Alanson White Psychiatric Foundation, 1947.

10. (*a*) Weinstein and Kahn.[8] (*b*) Freeman, W., and Watts, J. W.: Psychosurgery in the Treatment of Mental Disorders and Intractable Pain, Ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1950, pp. 139-140.

11. Weinstein and Kahn.[3] Freeman and Watts.[10b]

12. Petrie, A.: Personality and the Frontal Lobes: An Investigation of the Psychological Effects of Different Types of Leucotomy, Philadelphia, The Blakiston Company, 1952.

mood and psychomotor activity, and urinary incontinence. In prefrontal lobotomy and similar procedures the aim appears to be the production of a state of explicit verbal denial. Thus, in the successful case the patient is pictured as smiling, indifferent to his problems, and stating that there is nothing wrong and that he is getting along perfectly. When the expression of denial takes such implicit forms as restlessness, apathy, or alterations in sexual behavior, the result is regarded as an unsuccessful one. It is thus significant that the best results are reported as occurring in obsessional persons, i. e., in those in whom explicit verbal denial develops under the conditions of altered brain function.

SUMMARY

The premorbid personalities of 28 patients with brain disease who explicitly denied illness, including such disabilities as hemiplegia and visual loss and the fact that a craniotomy had been performed, are reviewed. The findings are compared with those in a group of 28 patients with comparable disabilities, similar lesions and electroencephalographic records, but without explicit verbal denial.

Explicit verbal denial occurred only in patients who had previously demonstrated certain personality attitudes. They were people with compulsive drives, a great need for prestige and the esteem of others, and a record of always having denied felt inadequacies. Illness was regarded as an imperfection which had to be denied or justified. Life experiences had been valued not for their intrinsic satisfactions but as a means of maintaining prestige and "security."

In the patients whose attitudes had been expressed predominantly in verbal symbols, in concern with "principles" and "being right," the denial was most complete and the mood was usually affable and serene. In the patients whose feelings were expressed in more "physical" symbols, relating especially to the body, food, and sexual activity, denial was less complete and the predominant mood was paranoid.

Explicit verbal denial is only one of the symbolic expressions of denial. Implicit manifestations include drowsiness and muteness, certain motor acts, alterations in sexual behavior, and the use of humor. While an altered milieu of brain function is necessary for the existence of all these patterns of denial, the choice of the particular element is determined by personality factors.

ADRENOCORTICAL RESPONSIVITY TO ELECTRIC SHOCK THERAPY AND INSULIN THERAPY

A Study of Fifty-Six Mentally Ill Patients in Rockland State Hospital, Orangeburg, N. Y.

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THE ROLE of the endocrine factor in the pathogenesis of psychosis has long been postulated. The possible relation of endocrine dysfunction to mental disorder may be seen in different ways: 1. The endocrine disorder may cause the mental disease. 2. The endocrine disorder may be a result of the mental disease. 3. The mental disease may be psychogenic, or in response to worry over the physical changes induced by the gland. 4. The mental disease and glandular dysfunction may coexist independently. Special attention has been given to the anterior lobe of the pituitary and the adrenal cortex.

Functional disturbances may be correlated with hyperfunction, hypofunction, dysfunction, or disequilibrium of the endocrine system. Castor and associates [1] gave large doses of cortisone to rats and found, on microscopic examination, evidence of damage to the thalamus, hypothalamus, and cerebral cortex. In Cushing's syndrome (adrenal cortex hyperfunction), which is due to a tumor or to hyperplasia of the adrenal cortex, mental derangements are fairly common. About 20% of patients exhibit psychotic symptoms with increased activity of the gland, or symptoms may occur in others as a psychogenic response to the physical manifestations of the disease, such as disfigurement, chronic invalidism, hirsutism, or acne.[2]

In Addison's disease, melancholia, depression, and confusional states are observed. Some authorities suggest the presence of functional adrenal cortex insufficiency in psychopaths. It is claimed that such patients manifest not hyperglycemia, but rather, hypoglycemia, in response to stress. The hypoglycemia which may develop is due to a decreased discharge of the adrenal cortex or to an increased insulin secretion. Large doses of cortisone, administered to apparently normal subjects, will cause metabolic changes, as well as mental disturbances.

Altschule and Grunebaum [3] report an interesting observation on sodium elimination through the perspiration of psychotic persons. They found that this elimination is increased in psychotic patients who have been ill more than three years, and that

1. Castor, C. W.; Baker, B. L.; Ingle, D. J., and Li, C. H.: Proc. Soc. Exper. Biol. & Med. **76**:353-357 (Feb.) 1951.

2. Trethowan, W. H., and Cobb, S.: A. M. A. Arch. Neurol. & Psychiat. **67**:284-309 (March) 1952.

3. Altschule, M. D.; Promisel, E.; Parkhurst, B. H., and Grunebaum, H.: Arch. Neurol. & Psychiat. **64**:641-649 (Nov.) 1950.

it is normal or elevated in patients sick for a shorter period. After insulin treatment, electric convulsion therapy, and spontaneous remissions, the sodium level in the sweat reverts to normal. This fact suggests that in patients with chronic psychoses the production of hormones controlling the electrolyte balance is diminished, since treatment stimulates the production of these hormones.

Friedlander and associates [4] report that elimination of glucocorticoids is remarkably increased in psychotic patients who respond favorably to electric convulsion therapy.

Selye [5] claims that repeated alarm stimuli associated with alcoholism may lead to various stages of adrenal cortex insufficiency and that this effect is the rationale of treatment of chronic alcoholism with cortisone, which may act as a substitute therapy.

In order to evaluate the relation of somatic therapy—in this case, electric convulsion therapy, or insulin and electric convulsion therapy—to the function of the adrenal cortex in psychotic persons, and to find out whether the changes in the function of the adrenal cortex caused by somatic therapy are related to the patient's prognosis, we undertook this project. The function of the adrenal cortex can be evaluated by a number of tests, since the adrenal cortex secretes a number of hormones and has several different functions. The hormones are divided into three large groups: hormones that influence the carbohydrate metabolism; hormones that influence the electrolyte metabolism, and sex hormones. While it is unlikely that only one function of the adrenal cortex may become abnormal, in rare cases a deficiency of a single factor may predominate. Tests based upon the response of the circulating eosinophiles are a measure of the carbohydrate-regulating factors of the adrenal cortex; tests based upon the urinary secretion of 17-ketosteroids are a measure of abnormal cortical androgen production; tests based upon water excretion are a measure of the electrolyte-regulating factors.

From examination of the function of one group of hormones, one has a general idea of the function of the adrenal cortex. We chose the eosinophile level of the blood as a measure of the function of the adrenal cortex because this test is a very simple one, does not require elaborate laboratory facilities, and is easy to perform on psychotic patients. Patients admitted to the hospital and recommended for electric convulsion therapy and/or insulin therapy were selected at random for this test.

METHOD AND MATERIAL

A fasting-blood sample was obtained from all subjects before the course of treatment was begun, and subsequent samples were taken at about two-week intervals. A quantitative eosinophile determination was made on each sample.

Examination of the blood was continued until the patient was placed on convalescent status or was transferred to another building as unimproved. These examinations give an indication of the function of the adrenal cortex, as evidenced by cellular changes in the patient's blood from soon after his admission to the hospital until a short time after termination of somatic therapy.

Fifty-six patients participated in this project—40 females and 16 males—and 380 tests were performed, approximately 7 tests for each patient.

4. Friedlander, J. H.; Perrault, R.; Turner, W. J., and Gottfried, S. P.: Psychosom. Med. **12**:86-88 (March-April) 1950.

5. Selye, H.: The Physiology and Pathology of Exposure to Stress: A Treatise Based on the Concepts of the General-Adaptation-Syndrome and the Diseases of Adaptation, Montreal, Canada, Acta, Inc., 1950, p. 673.

OBSERVATIONS

Of 56 patients undergoing somatic therapy, there was evidence of depressed function of the adrenal cortex, as measured by an increase in the eosinophile level of the blood, in approximately 44, or 80% (Table 1). Of these 44 patients with decreased function of the adrenal cortex due to somatic therapy, the condition of 75% was much improved or improved, and that of 25% was unimproved; that is, in 75% of the cases in which a decrease in the function of the adrenal cortex followed the therapy, this decrease was correlated with improvement in the patient's mental condition.

TABLE 1.—*Relation of Responsivity of Adrenal Cortex (Change in Eosinophile Level) to Change in Mental Condition*

	Eosinophile Count			
	Increase	Decrease	No Change	Total
Much improved	15	1	..	16
Improvement	18	4	..	22
Unimproved	11	2	5	18
Total	44	7	5	56

TABLE 2.—*Relation of Duration of Psychosis to Responsivity of Adrenal Cortex and Change in Mental Condition*

Status	Eosinophile Level			
	Increase	Decrease	No Change	Total
Sick Less Than Three Years				
Much improved	14	1	..	15
Improved	11	1	..	12
Unimproved	4	..	1	5
Total	29	2	1	32
Sick More Than Three Years				
Much improved	1	..	..	1
Improved	7	3	..	10
Unimproved	7	2	4	13
Total	15	5	4	24

This result is in line with investigations made by Sackler and associates,[6] who believe that the response of the adrenal cortex during therapy, as indicated by changes in the blood eosinophile level, has a prognostic value. Marked decrease in cortical activity is, according to them, correlated with clinical improvement. Accord- to their investigations, in the beginning of the treatment with insulin, electric shock, and histamine, there is an increase in the function of the adrenal cortex. Later in the course of the therapy there is evidence of decreased cortical activity. Five patients included in this project (Tables 1 and 2) showed no response in the eosinophile level after somatic therapy. This means that the adrenal cortex in these patients did not respond to the stress situation (shock treatments), and it is interesting to note that all five patients showed no change in their mental condition. Of the five patients, four had been sick more than three years and one less than three years. It is

6. Sackler, and others: Psychiatric Quart. **25**:213-236 (April) 1951.

possible that in these patients prolonged severe stress of an emotional nature had exhausted adrenocortical responsivity, or it might be that the psychosis itself, acting as a protective mechanism against conflicting life situations, blocked adrenocortical responsivity to stress.

Ebaugh and Bush [7] believe that the failure in the hormonal balance of schizophrenic patients is at the adrenal level, quantitatively and qualitatively, and not at the level of the anterior lobe of the pituitary. The assumption is based on the statement that in an experimental state of exhaustion corticotropin (ACTH) produces an adrenal response but that in a schizophrenic patient it will not.

As seen in Table 2, the duration of illness plays an important role in the responsivity of the adrenal cortex to somatic therapy. In approximately 90% of patients sick less than three years the somatic therapy had an antiadrenocortical effect. In slightly more than 60% of patients sick more than three years the somatic therapy had an antiadrenocortical effect. These results agree with the observations of Reiss and associates,[8] who investigated the responsivity of the adrenal cortex in relation to psychotic illnesses and found that patients with chronic schizophrenia showed significantly fewer positive responses to dextrose than did patients with active schizophrenia.

Similar observations were made in relation to physical diseases by Selye,[9] who stated that well-nourished subjects subjected to stress showed a marked increase in the urinary excretion of glucocorticoids, while in chronically ill, undernourished persons subjected to stress the rise in glucocorticoid excretion was slight or absent. According to him, the condition of the chronically ill patient corresponds to the stage of resistance in which corticoid secretion is probably less intense than during the stage of alarm.

In seven patients (Table 1) the function of the adrenal cortex increased during therapy, as evidenced by a decrease in the eosinophile level of the blood. Of the seven patients, two were sick less than three years and five more than three years. One was placed on convalescent status as much improved; four maintained their improvement, and two were unimproved. It is possible that in these patients either the somatic therapy was not intensive enough, since, as is known, the function of the adrenal cortex usually increases at the beginning of the treatment, or the function of the adrenal cortex was so disorganized that it responded to an antiadrenocortical stimulant with an increase of function. It is interesting to note that of the seven patients, five had electric convulsion therapy and two insulin therapy with electric shock; as is known, electric shock therapy is a less intensive treatment than insulin with electric shock. Of the seven patients, two had only three electric convulsion treatments, and one was a drug addict.

There is no difference in the responsivity of the adrenal cortex with relation to the sexes (Table 3). In 80% both of the females and of the males, the somatic therapy had an antiadrenocortical effect.

A difference was shown in the adrenocortical responsivity between patients receiving only shock treatment and those receiving insulin and electric shock therapy (Table 4). Of 43 patients receiving insulin plus electric shock, the somatic

7. Ebaugh, F. G.: Am. J. M. Sc. **221**:108-112 (Jan.) 1951.

8. Reiss, M., and others: J. Clin. & Exper. Psychopath. **12**:171-183 (July-Sept.) 1951.

9. Selye,[5] p. 223.

therapy had an antiadrenocortical effect in 38, or in approximately 88%. Approximately 7% of the treated patients showed no adrenocortical response to somatic therapy, and in seven patients, or approximately 5%, the somatic therapy had a rather stimulating effect on the function of the adrenal cortex.

TABLE 3.—*Relation of Sex to Responsivity of Adrenal Cortex to Change in Mental Status*

Status	Eosinophile Level			
	Increase	Decrease	No Change	Total
Females	8	..	..	8
Males	7	1	..	8
Improved				
Females	13	3	..	16
Males	5	1	..	6
Much improved				
Unimproved				
Females	11	..	5	16
Males	..	2	..	2
Total				
Females	32	3	5	40
Males	12	4	..	16

TABLE 4.—*Relation of Adrenocortical Responsivity to Change in Mental Status for Patients Receiving Electric Convulsion and Insulin Therapy and Patients Receiving Electric Convulsion Therapy Alone*

Status	Eosinophile Level			
	Increase	Decrease	No Change	Total
Electric Convulsion and Insulin Therapy				
Much improved	12	..	..	12
Improved	16	1	..	17
Unimproved	10	1	3	14
Total	38	2	3	43
Electric Shock Therapy Only				
Much improved	3	1	..	4
Improved	2	3	..	5
Unimproved	1	1	2	4
Total	6	5	2	13

TABLE 5.—*Relation of Adrenocortical Responsivity to Type of Psychosis*

Psychosis	Eosinophile Count			
	Increase	Decrease	No Change	Total
Dementia praecox, catatonic	15	1	2	18
Dementia praecox, paranoid	17	3	..	20
Dementia praecox, mixed	5	2	1	8
Dementia praecox, hebephrenic	3	..	1	4
Manic-depressive, depressed	3	..	..	3
Involutional, paranoid	..	..	1	1
Involutional, melancholia	1	1	..	2
Total	44	7	5	56

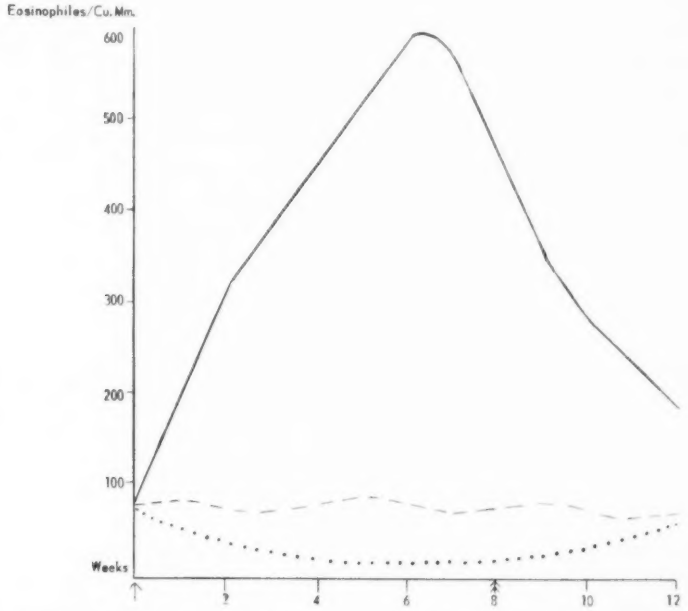
Of 13 patients receiving electric shock therapy, the treatment had an antiadrenocortical effect in approximately 45%. In about 40% the somatic therapy stimulated, and in about 15% it had no influence on, the function of the adrenal cortex.

There was apparently no relation of the adrenocortical responsivity to the diagnosis (Table 5).

In our investigations, there was no correlation between the degree of depression of the function of the adrenal cortex and the extent of the patient's mental improvement. The average variation in the eosinophile level is presented in the Chart for the three groups, namely, those with an increase, those with a decrease, and those with no change in the count.

SUMMARY

A study of the adrenocortical responsivity to insulin and/or electric convulsion therapy in 56 patients in a state hospital is presented. The relations of the adrenocortical response to duration of illness, sex, type of treatment, and prognosis are discussed. Of the 56 patients receiving somatic therapy, approximately 91% had



Average circulating eosinophile level, per cubic millimeter, before, during, and after electric shock and/or insulin therapy. Values for the 44 patients who had an increase in the eosinophile level are shown by solid line; values for the 5 patients who showed no response in the eosinophile level, by the broken line, and values for the 7 patients who showed a decrease in the eosinophiles by the line of dots. The arrow indicates base level before treatment, and the point at which treatment was begun; the double arrow, cessation of treatment.

a responsive adrenal cortex. Approximately 9% showed no response in the function of the adrenal cortex. Of approximately 91% of the patients in whom the somatic therapy influenced the adrenal cortex, the somatic therapy had an antiadrenocortical effect in approximately 80%, and a stimulating effect on the adrenal cortex, as evidenced by the cellular changes, in approximately 11%. Of the approximately 9% in whom the adrenal cortex was unresponsive, all remained unimproved. Of the 80% of patients in whom the somatic therapy had an antiadrenocortical effect, approximately 75% showed improvement in their mental condition with 15 patients much improved and 18 patients improved.

Although a functional disease may be a result of or a cause of, or may have no direct relation to, an unresponsive adrenal cortex, the eosinophile level may give a clue to the patient's prognosis, based on the function of the response of the adrenal cortex to stress (somatic therapy).

In general, it can be stated that a fair prognosis can be expected in patients on whom the somatic therapy had an antiadrenocortical effect, and that patients with an adrenal cortex unresponsive to somatic therapy have a poor prognosis. There is no correlation between the degree of the depression of the function of the adrenal cortex and the extent of the patient's improvement.

Mr. Allan Hennessey, Senior Medical Technician, performed the blood tests in this investigation.

TIC DOULOUREUX OF THE CHORDA TYMPANI

Report of Cases

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HUNT[1] IN 1907 first described what he called geniculate neuralgia after his observation of herpes together with sensory changes and pain accompanying peripheral facial paralysis. He stated that the primary disorder was in the geniculate ganglion and compared it with the motor and sensory phenomena of Gasserian ganglion neuralgia. He outlined the anatomic area and called it the "geniculate zone," a cone-shaped area including the drum membrane, the external auditory canal, the entrance to the canal, and the concha, tragus, antitragus, and antihelix. He stated that the 9th and 10th cranial nerves contribute to sensation in this area.

Clark and Taylor,[2] in 1909, reported a case of tic douloureux involving the sensory portion of the seventh cranial nerve (nervus intermedius). His patient, a woman aged 28, had severe tic-like spasms of pain immediately in front of the left ear for two years and a steady pain deep in the ear and on the anterior wall of the external auditory canal. The diagnosis was tic douloureux of the geniculate system. He therefore exposed the lateral lobe of the cerebellum, opened the dura, exposed the cerebellopontine angle, and sectioned the facial nerve, the nervus intermedius, and the upper portion of the eighth nerve. The patient was relieved of the pain at once. She was observed for six years after the operation, with no recurrence of pain.

This was the only undisputed case in the literature until 1933, when Reichert[3] reported a similar one in which the attacks were of "sharp, stabbing pain deep in the external auditory canal, causing the patient to shriek out and grab her ear." Reichert thought that this was another case of geniculate neuralgia, since the symptoms were almost identical with those in the original case described by Clark and Taylor. With local anesthesia, he exposed the lateral lobe of the cerebellum, opened the dura, and exposed the cerebellopontine angle. When he touched the

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1. Hunt, J. R.: Herpetic Inflammations of the Geniculate Ganglion: A New Syndrome and Its Aural Complications, Arch. Otolaryng. **36**:371, 1907; Herpetic Inflammations of the Geniculate Ganglion: A New Syndrome and Its Aural Complications, J. Nerv. & Ment. Dis. **34**:73, 1907; The Sensory System of the Facial Nerve and Its Symptomatology, ibid. **36**:321, 1909; A Further Contribution to the Herpetic Inflammations of the Geniculate Ganglion, Am. J. M. Sc. **136**:226, 1908.

2. Clark, L. P., and Taylor, A. S.: True Tic Douloureux of the Sensory Filaments of the Facial Nerve, J. A. M. A. **53**:2144 (Dec. 25) 1909.

3. Reichert, F. L.: Tympanic Plexus Neuralgia: True Tic Douloureux of the Ear or So-Called Geniculate Ganglion Neuralgia, J. A. M. A. **100**:1744, (June 3) 1933.

seventh and eighth nerves, there was pain in the auditory canal, not the typical tic-like pain complained of by the patient. Touching the ninth nerve produced the identical tic-like pain complained of. Section of the ninth nerve relieved the pain completely. Reichert described two types of glossopharyngeal neuralgia.

> The common or complete tic douloureux of the glossopharyngeus is characterized by paroxysms of lancinating pain, starting in the tonsillar fossa or base of the tongue, generally radiating deeply in the ear, accompanied by salivation and induced by swallowing, talking or other movements of the throat or tongue.
>
> The partial or Jacobson's plexus tic douloureux of the glossopharyngeus is characterized by paroxysms of lancinating pain in and about the external auditory canal and is not induced by any movements of the pharynx or tongue and is not accompanied by salivation. This neuralgia has heretofore been considered as a geniculate ganglion neuralgia.
>
> Intracranial division of the glossopharyngeal nerve has cured both types of these neuralgias.

Furlow,[4] in 1942, described a patient with severe tic-like pain in the ear who was completely relieved by section of the nervus intermedius. The patient, a young girl, complained of spasmodic severe pain deep in her ear of two years' duration. She had no pain in her throat, and the pain was not produced by swallowing. Occasionally there were left-sided headache and pain radiating to the left eye. Neurologic and all other examinations revealed nothing significant. There was a very sensitive area in the posterosuperior portion of the left external auditory canal close to the drum membrane. When this area was touched, the tic-like pain was produced. She sought relief at any cost. She was told that the only certain method of differentiating glossopharyngeal neuralgia and geniculate neuralgia was to stimulate each nerve separately to see which one produced the tic-like pain. She was also told that it might be necessary to sacrifice a part of the eighth and the motor root of the seventh nerve in order to obtain relief from the pain, and to all of this she willingly agreed.

With local anesthesia, Furlow exposed the lateral lobe of the cerebellum, opened the dura, and exposed the cerebellopontine angle. When the ninth nerve was touched, the patient experienced pain in her throat, which radiated to her ear, but this was not the typical tic-like pain she complained of. When the nervus intermedius was isolated and picked up with a blunt hook, the patient complained bitterly of the tic-like pain, in the ear, identical with the pain she complained of. As the nervus intermedius was sectioned, she cried out with pain, but the pain ceased immediately. The sensitive area on the posterosuperior canal wall close to the drum membrane was no longer sensitive. Taste sensation on the anterior two-thirds of the tongue on the left side was lost for bitter, sweet, salt, and sour. Rosen[5] and Costen, Clare, and Bishop[6] induced severe pain in the ear by stimulating the chorda tympani. Section of the chorda results in loss of taste sense on the anterior two-thirds of the tongue on the same side, just as when the nervus intermedius is sectioned. The chorda tympani, as well as the nervus intermedius, is a mixed sensory nerve. The two nerves may be regarded as one.

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4. Furlow, L. T.: Tic Douloureux of the Nervus Intermedius (So-Called Idiopathic Geniculate Neuralgia), J. A. M. A. **119**:255 (May 16) 1942.

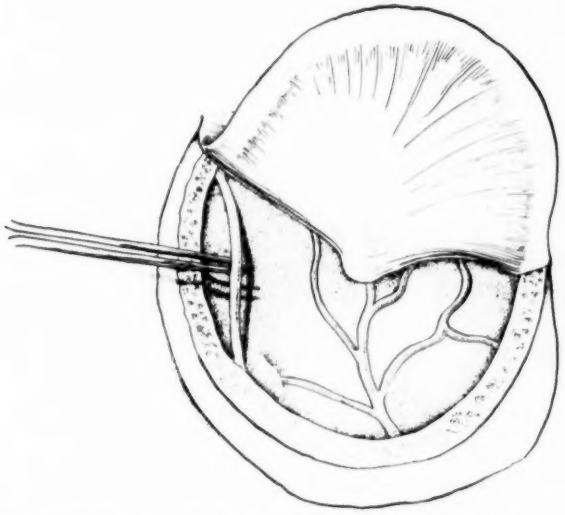
5. Rosen, S.: Surgery in Ménière's Disease: A New Operation Which Preserves the Labyrinth; Report of Cases, Ann. Otol. Rhin. & Laryng. **60**:657 (Sept.) 1951.

6. Costen, J. B.; Clare, M. H., and Bishop, G. H.: Transmission of Pain Impulses via the Chorda Tympani Nerve, Ann. Otol. Rhin. & Laryng. **60**:591 (Sept.) 1951.

In the following two cases the patients had severe tic-like pain deep in the ear for two to three years, and the symptoms were very similar to those reported by Clark and Taylor [2] and Farlow.[4] In these cases the pain was relieved completely by section of the chorda tympani.

REPORT OF CASES

CASE 1.—Mrs. H. S. was referred by Dr. Meyer Rosenberg, neurosurgeon, on May 14, 1952. For the previous three years she had had sharp, tic-like, shooting pain deep in and about her left ear, involving the external canal and the entire pinna. The spasms of intolerable pain lasted from 1 to 12 hours. In the beginning the attacks occurred every two to three months, then more frequently, and in the past 10 months three to four times a week. Pressure and heaviness in the head accompanied the pain. Swallowing, talking, yawning, biting, or chewing did not precipitate the pain.



After the drum membrane is lifted out of its sulcus, it is folded upward, thus exposing the chorda tympani, which is seen resting on the bipolar electrode during electrical stimulation. The grooves on the inner tympanic wall containing Jacobson's nerve and other branches of the tympanic plexus can be seen.

There had been no diplopia, syncope or convulsions; olfactory, auditory, or visual hallucinations; limb weakness, or sensory disturbance. The drum membranes and auditory canals were normal; hearing and caloric tests gave normal responses. X-rays of the skull and the internal auditory canals showed nothing abnormal. The blood pressure was 110/70. Psychiatric examination revealed a stable, sincere person, without any emotional basis for the pain.

On June 4, 1952, with local anesthesia, the skin of the external auditory canal was incised from 3 to 9 o'clock about 6 mm. external to the drum membrane. The skin was separated as far as the drum membrane. The membrane was lifted out of its sulcus and folded upward upon itself, like an apron, thus exposing the tympanic cavity. The chorda tympani and Jacobson's nerve came into view at once. (This technique has been employed by Rosen [5] in treating Ménière's disease.) Jacobson's nerve and the chorda tympani were stimulated separately. A square pulse stimulator, capable of independent variation of pulse width and strength, was used, with pulses of 0.3 msec. at 50 cps per second. When the bipolar electrode came in contact with Jacobson's nerve the patient said, "I feel a deep pain in the back of my throat

and left ear." The pain in the ear in no way resembled her tic-like pain. When the chorda tympani was similarly stimulated, she said, "That is exactly like my ear pain," and with each stimulation she said, "I hear a buzzing sound in my ear and feel something on the left side of my tongue."[7] When the chorda tympani was sectioned, she shrieked with pain, saying, "That is the identical pain which I always have with my attacks." The pain diappeared completely, and there has been no recurrence. The drum membrane and skin of the canal wall were then replaced in their former position. The patient left the hospital the following day (Figure).

CASE 2.—Mrs. Y. L., aged 28, was seen in Tel Aviv in August, 1952, while on a medical mission for the Israeli government. For the past two years she had suffered attacks of sharp, tic-like, exquisite pain deep in the right ear and in the external auditory canal. The episodes occurred daily and were extremely painful. General physical and laboratory examinations revealed nothing abnormal. With each attack of severe tic-like pain she had tinnitus in the right ear, slight vertigo, and a bitter taste. On Aug. 13 the same procedure was performed in this case as in Case 1. She shrieked with pain only when the chorda tympani was pulled upon. The nerve was sectioned. Since then there has been no recurrence of pain.

The method used here to determine differentially whether the seventh or the ninth nerve is responsible for the tic-like pain is unique. These cases are reported so soon after section of the chorda tympani because they seem to establish that tic douloureux of the chorda tympani exists and may be abolished by section of that nerve. Differential stimulation of the seventh and ninth nerves in the tympanum to determine which nerve is to be sectioned is a much simpler approach than stimulation by the intracranial route.

CONCLUSIONS

1. Tic douloureux of the chorda tympani is a clinical entity.

2. Tic-like pain in the ear may be abolished by section of the nervus intermedius, the chorda tympani, or the glossopharyngeal nerve.

3. The nerve responsible for the tic-like pain can be determined by differential stimulation in the tympanum.

101 East 73d St.

7. Rosen, S.: Surgery and Neurology of Ménière's Disease: Role of the Chorda Tympani Nerve in Tinnitus, Vertigo, and Deafness, A. M. A. Arch. Otolaryng. **56**:152 (Aug.) 1952.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

William Malamud, M.D., Presiding
Regular Meeting, May 26, 1952

Clinical Associations of Electroencephalographic Foci in the Temporal Lobe. Dr. Denis Hill, London, England.

The clinical associations of patients showing electroencephalographic foci in the anterior part of the temporal lobe were compared with those of patients having foci in the posterior part. The present series included 56 cases of foci in the anterior part and 61 cases of foci in the posterior part. Bipolar-electrode technique with pharyngeal and "sphenoidal" needle electrodes was used, the later being employed frequently in association with barbiturate-induced sleep. The focal disturbances consisted of spikes, sharp waves, rhythmic 4- to 6-cps waves, and rhythmic 3- to 5-cps waves of larger amplitude; these might be unilateral or bilateral. The patients were largely obtained from Maudsley Hospital, London, and the majority were studied as inpatients. Since the case material was psychiatric, only a small number (less than 10%) had gross brain pathology. The great majority of the patients with anterior lesions, but only 33% of the patients with posterior lesions, had clinically recognized epileptic seizures, usually psychomotor automatisms. Major seizures, when present, occurred during sleep in most cases. The presence of a spike focus as the only electroencephalographic abnormality on the inferior surface of the temporal pole was evidence against a gross lesion. The spike type of focus was commoner anteriorly than posteriorly; slow rhythmic waves were common in the posterior temporal areas. Evidence was found for associating these foci with cerebral maturation defects. The development of such foci has been observed in late childhood, and in early childhood a phase of development is passed through in which they may be "physiologic." In adult life the presence of temporal foci of either type is associated with serious psychiatric disabilities in 50% of cases, but these disturbances are more serious with the posterior foci. Psychopathic aggressive behavior, antisocial conduct, late enuresis, twilight states, periods of confusion with psychotic behavior, and homicidal and suicidal attempts are commoner with the posterior than with the anterior foci. The serious psychiatric disorders associated with epilepsy, heterogeneous in symptomatology as they may be, appear to have a common factor in an excitable focus in the temporal cortex in the majority of cases.

DISCUSSION

Dr. William Malamud: Dr. Hill is to be thanked for a comprehensive, systematic, and clear presentation of the present status of electroencephalography in the study of human behavior. I know of nothing that has made such spectacular contribution to this field as has electroencephalography. Those of us who have followed this work from its inception can remember the brilliant address by Dr. Adrien at the meeting of the American Neurological Association in 1934 and his admission that he had originally doubted the value of this method but had subsequently come to be one of its exponents. It is of particular interest to us to take cognizance of the fact that one of our colleagues in Boston has anticipated the importance of electroencephalography even before the publications of Berger; I should like Dr. MacPherson to tell us about his early contribution to this subject.

Dr. Donald J. MacPherson: The difficulty in having anticipated all this activity and recorded the first brain wave was that when we got it we did not know what we had. The film was placed on file. Much later, when, with more sensitive recording, enthusiasm for this type of investigation established the fact and significance of brain waves, it came to light that these waves were present in the original film. These records are all on display at the Warren Museum. This evening's presentation represents a high point in the recording of this phenomenon and its interpretation. It has been a moot point as to what correlations exist

between brain waves and behavior and the deductions one could draw. The correlations indicated in Dr. Hill's paper seem to be significant, and I think we can agree with the conclusions that have been made. It has been a rewarding experience.

DR. ROBERT S. SCHWAB: Dr. Hill has made an interesting presentation and emphasizes the complexity of the temporal lobe, a common meeting ground of psychiatry and neurology, where the clinical pattern of the seizure is not as well defined as in grand mal or petit mal. Of interest to me is the question why these temporal lobe seizures are so resistive to therapy. Does Dr. Hill have any explanation? Is there something specific about the temporal lobe, or the fact that there are two temporal lobes, that is involved in making these spells so difficult to treat?

DR. WILLIAM MALAMUD: At the dedication of the laboratory at the McLean Hospital, Dr. Gasser suggested that one of the most promising fields in the study of human behavior was that which deals with the metabolism of the central nervous system. We have Dr. Hudson Hoagland here, who has made important contributions to the study of brain metabolism and electroencephalography.

DR. HUDSON HOAGLAND: I should like to ask Dr. Hill whether there is evidence that metabolic disturbances, including endocrine factors, may be correlated with the various electroencephalographic abnormalities he has described.

DR. WILLIAM MALAMUD: One of the most important applications of this method of investigation is in the study of epilepsy, and I shall call on Dr. Merlis to discuss this phase.

DR. JEROME K. MERLIS: Dr. Hill has pointed out that the focus in the anterior portion of the temporal lobe was unilateral in 75% of his cases. In our material we have found that with repeated sleep studies it has been possible to demonstrate bilateral foci in up to 85% of the cases. Sometimes it has taken as many as six sleep records to demonstrate the focus on the other side. The two foci appear to operate independently. One wonders about the cause of these foci and about their connection with the seizures. It has been our experience that ablation of the anterior portion of one temporal lobe may control the seizures, although the spike focus in the anterior part of the temporal lobe of the other side is still present. Dr. Hill recently asked me whether I had any theory to explain this. I replied that I had several, none of which was satisfactory. I should now like to ask the same question of Dr. Hill.

DR. SAMUEL GROSSMAN: I have a question concerning maturation and abnormalities. Do they have any subcortical or cortical origin?

DR. CHARLES S. DAVIDSON: I wonder whether there is a similar abnormality in patients who have episodic disturbances of behavior and foci of the posterior portion of the lobe.

DR. DENIS HILL, London, England: It was a very great pleasure to hear Dr. MacPherson, whose original early observations are not generally known outside this country, and have certainly not yet received the recognition in the history of the subject which they deserve. Dr. Schwab's question about therapy is one he knows I cannot answer. An answer he himself could give is that we have not yet found a drug to control this type of epilepsy. Some people think we have found a drug for other types of epilepsy. We do know some of them are effective, but the seizures referable to the anterior portion of the temporal lobe are often resistant to all drugs. Perhaps these seizures are the end-result of an epileptic process which initially was seen as more diffuse. How this comes about we do not know at all.

As to Dr. Hoagland's question, I have no direct evidence that metabolic or endocrine factors affect the excitability of these foci. However, many of the patients have their seizures at the menses, but one could say that about epilepsy in general. Psychotic episodes have occurred in epileptic patients during menstruation, and these usually have been associated with temporal electroencephalographic foci, suggesting that the excitability of these foci is susceptible to metabolic change. They are certainly susceptible to hypoglycemia and anoxia.

Dr. Merlis made an interesting observation, i. e., that the unilateral foci, if studied long enough, are found to be bilateral. We have not done as many repeat studies as he has. It is of great interest that he finds that in 85% of his cases the foci are found to be bilateral if studied long enough. This supports the idea that the focus on one side may excite a focus on the other side. Whether this occurs, or whether both are excited by a third excitable zone, we cannot say. Experimental work on animals indicates that spike discharges of the temporal poles

can be induced by stimulating certain deep central areas of gray matter, e. g., the septal nuclei. This is an equally good explanation for the production of bilateral foci. The question of the cause of these foci is a difficult one. Of our patients, drawn largely from a psychiatric clinic, only a small proportion (less than 10%) have been associated with gross lesions. We have three temporal lobes removed that have proved normal, microscopically and macroscopically. Undoubtedly, these areas of abnormal excitability can occur in histologically normal cortex.

Dr. Grossman's question is one we cannot answer until we can make electrocorticograms. On the basis of the physical character of these foci, one assumes that the disturbance itself is of cortical origin, but this does not exclude a subcortical pacemaker or exciting focus. I am not certain I understood Dr. Davidson's question. The posterior foci are definitely associated with aggressive episodic behavior.

DR. CHARLES S. DAVIDSON: Have you any ictal electroencephalograms?

DR. DENIS HILL, London, England: We have not recorded a seizure starting from a posterior temporal focus, nor have we recorded the electroencephalogram during episodes of behavior disturbance in such cases. One cannot make a recording during the time a man attacks his wife. With the posterior temporal foci one does not find the short-term disturbance which occurs with anterior foci and which clinically makes the diagnosis of epilepsy easier.

Equation of Mind with Brain. DR. F. M. R. WALSHE, London, England.

In a recent symposium on cerebral mechanisms in behavior, a speaker expressed the view that all the participants subscribed to the faith that the phenomena of behavior and of mind are ultimately describable in terms of the mathematical and physical sciences.

It is noteworthy that in general physicists do not entertain this bleak hope, for, as a distinguished mathematician has remarked, "they see more clearly than other people the impossibility of explaining spiritual values in terms of electrons and protons."

If there exist spiritual, moral, and esthetic values, the notion that they can be regarded as merely the activity of nerve nets is one that has nothing in philosophy or in natural science to commend it. The suggestion that man will ultimately be most adequately accounted for in terms of mathematical and statistical formulae is the negation of biology and the end of psychology. Man is something more than a focus for the hurrying to and fro of molecules, and his mind something more than a bloodless dance of action potentials.

We may admit that brain is an organ of mind, but that there is no other valid universe of discourse about mind than that of natural science is an assumption that has nothing scientific about it.

The claim that nerve nets can know universals is based upon a naïve confusion of generals with universals, and those who make the claim do not understand the terminology they use. A "general" is a term applicable to any one of an indefinite number of objects which resemble each other in certain qualities. A "universal" is a concept embracing the essence, being, or nature of a thing—that without which it would not be what it is. This universal is the primary datum of the intellect, and there is no evidence of any kind that nerve nets can know universals, though they can know generals.

It has yet to be discerned what relation cybernetics has to the nervous system. Its terminology may be no more than a new symbolic logic in terms of which many logical statements can be made: a dialectic with no known relation to biology.

DISCUSSION

DR. WILLIAM MALAMUD: Thank you, Dr. Walshe, for a most stimulating and thought-provoking presentation on a subject which has occupied the minds of men ever since they began to think. As you have brought out in your comprehensive survey, there is a vast range of variety in the ways in which the problem has been dealt with through the ages. I presume there will also be differences of opinion and attitudes expressed by those present tonight. For myself, I missed in your historical survey reference to the definition of mind (psyche) which Plato attributes to Socrates in the "Theaetetus." In regarding "psyche" as an integrating mechanism of human functions (physiological and psychological) he succeeds, to my satisfaction, in doing away with the dualism of mind and body. It is true that at this time we are not as yet prepared to demonstrate the intricate relationship of human behavior as a holistic function to the more specific functions of the central nervous system. This, however, need not discourage

us from working toward such a goal, keeping in mind Browning's "Ah, but a man's reach should exceed his grasp, or what's a heaven for?" I am certain that Dr. Denny-Brown could speak more effectively on this.

DR. D. DENNY-BROWN: I should like to put the proposition to Dr. Walshe that a mechanism of progressive signaling can exist at a perceptual level. Some of you recall at the March meeting we discussed a case of a parietal lesion in which the patient was unable to feel pain because the painful stimulus did not cover a sufficient area. Yet the patient was able to think of pain, could feel pain, could manipulate the idea of pain. I should feel, therefore, that in relation to that patient the stimulus quality of pain was not adequately perceived, though pain could exist as a mental process. It has always intrigued me that certain behavioral mechanisms proceed on a progressive basis to a point where ultimately there is a biological action which completes a cycle. The conditioned reflex of Pavlov is such a cycle. The satisfaction of the response by feeding the animal completes the cycle which conditioning had set up. It is also obvious in relation to the phenomenon of instinctive grasping, which is a simple progressive tropism. The hand extends and the limb extends, at right angles to the last touch. If the movement succeeds in producing another contact, then a further movement is induced, and ultimately the limb is rotated to bring the last stimulus toward the palm of the hand. It is possible to account for a series of complex movements in space that succeed in the grasping of the object. Cybernetics uses such a mechanism to explain behavior, but such a mechanism still leaves unexplained the properties of mind, thought, and memory. Mind is a further distillation of neuronal activity involving perhaps another dimension.

DR. WILLIAM MALAMUD: I regret that we cannot call upon most of the persons whom Dr. Walshe cited. We do have Dr. Brazier with us, and I should like to have her discuss this paper.

DR. MARY A. B. BRAZIER: I found this a stimulating and exciting talk, for science flourishes on controversy and Dr. Walshe has certainly made some controversial points. Some of our differences are terminologic, but some real issues have been raised that would have been interesting to discuss. Those of us who begin to explore in terms of a new discipline realize from the history of science that we have to expect attack. Dr. Walshe has, by a verbalism, disparaged the open mind, but he cannot take from us our inquiring minds. Gerard has said that in the first half of this century people who worked in my field were much concerned with the blood-brain barrier. It begins to look as though in the second part of the century the work would be on the "mind-brain" barrier!

DR. WILLIAM MALAMUD: I should like to call on Dr. Cobb, who has contributed a great deal to the clarification of the problem of the mind-body dualism.

DR. STANLEY COBB: This has been a red-letter evening, and one which the Society will long remember, for we do not often have a chance to hear two such famous speakers from the old school in England, where we have learned so much. We all admire Dr. Walshe as the man who has upheld standards in neurology by being perfectly willing to be critical. I do not mind saying that I have been afraid of his sharp pen for 25 years!

This evening I would be foolish if I went into a discussion of his paper, after hearing it only once. One should have such a paper a month. But I shall pick out several points. Like Dr. Walshe, I have faith—a faith that a scientist does not have to invoke the supernatural to understand how the brain works. I do not think that Dr. Walshe ought to be so hard on the cybernetics group, who have conceived a very interesting analogy. It is only an analogy up to now, but a stimulating one, and in some lines exciting. I think Dr. Walshe was not altogether accurate when he said that we who are interested in cybernetics take it as "a complete explanation of the mind." It is much less than that. Let me mention one specific contribution: It has proposed a theory for memory. That is something of an achievement. Until this was offered, all the explanations of memory had been so naive or vague that they were useless. This one is a possibility. I would not scoff at cybernetics as Walshe does. I would let cybernetics have a show. What we all really want to know is how the brain works; and it is my belief that when we know that, we will know what mind is.

DR. HARRY C. SOLOMON: I should think that this paper was a confession of faith, which is hard for me to debate. Man has been searching for generations to get an understanding of mind and almost always gets involved with the problem of the soul, which he assumes dis-

tinguishes man from other animals. As for my own confession, may I say that I have never been able to comprehend certain philosophical concepts, such as infinity and the boundaries of time and space. Similarly, I have been able to comprehend the mind only as a function of the brain, but this is a use of words that gets me no great distance. Bearing in mind Dr. Denny-Brown's pertinent remarks about the open mind, I fear that I cannot agree wholeheartedly with Dr. Walshe, Dr. Brazier, or Professor Northrop. It is my opinion that an attempt to study the laws of brain function as they relate to what I think of as the mind is one of the challenging efforts of man, but at the present moment it has not reached a point where it can be considered a finished project. Indeed, each and any of us may be on the wrong road. However, until the road is followed to its conclusion, it is premature to say that such a road will lead nowhere. There are a number of roads that may be traveled when one is trying to understand mind. Somewhere, sometime, these may come together. Meanwhile, I hope that more debates in this area can be carried on, but would hope to have a little more preparation before attempting to answer such masterly marshaled remarks as those of Dr. Walshe.

DR. WILLIAM MALAMUD: I sympathize with Dr. Brazier in wishing Northop were here, and that Weiner were here, too. The only person who has ever been able to make sense out of cybernetics for me has been Dr. Hoagland, who has discussed the matter with me from time to time. I should like to ask him to comment on Dr. Walshe's paper.

DR. HUDSON HOAGLAND: I fear that Dr. Malamud has considerably overestimated my competence in relation to cybernetics, but there are some things I should like to say in response to Dr. Walshe's exciting paper.

If we trace the course of biological science into the past, we find the trail scattered with the wreckage of vitalistic hypotheses which have been discarded as fruitless in advancing our knowledge of living organisms. Thus, prior to Wöhler's synthesis of urea, in 1828, it was firmly believed that the carbon compounds were not subject to the laws of chemistry and that special vital forces were required for their reaction, which put them in a class by themselves. These mystical immeasurable properties received a death blow from Wöhler's synthesis, after which organic chemistry, as we know it today, was born. Once the vitalistic brakes on organic chemistry and its 20th-century offspring, biochemistry, were removed, these disciplines flowered with vigor, and the impact of these disciplines on science, medicine, industry, and society needs no belaboring before this group. In a like manner, vitalistic concepts so prevalent in biology even a few decades ago, such as Driesch's concept of entelechy in embryology, have been increasingly discarded because of their sterility as hypotheses.

While electrophysiology dates from Galvani's experiments, in 1786, it has only been since 1920 that modern electronic concepts and tools have been available to furnish a new impetus to studies of the physiology of the nervous system. It is thus hardly surprising that this difficult and complex field is as yet scarcely within hailing distance of the practical problems of clinical neurology, psychiatry, and animal behavior. The views of the proponents of cybernetics have seemed to me to furnish stimulating hypotheses to be tested experimentally, and the value of these hypotheses can only be judged at some future time, in terms of experiments yet to be done. The concept of purpose in behavior has, for example, never been possible to handle in the laboratory. The idea of negative feed-back furnishes an interesting operational approach to purposive behavior, both in animate and in inanimate systems. The significance of negative feed-back in relation to purpose will, indeed, be interesting to examine a decade or a generation hence.

CHICAGO NEUROLOGICAL SOCIETY

Hugh T. Carmichael, M.D., *President, in the Chair*

Regular Meeting, Oct. 14, 1952

Paralysis of Bulbar Musculature in Certain Muscular Diseases. DR. IRVING C. SHERMAN and DR. LOUIS D. BOSHES.

Six cases were presented in which there was impairment of one or more parts of the musculature of the glossopharyngeolaryngeal apparatus in diseases which supposedly attack the muscles peripherally.

Four patients suffered from dermatomyositis. Two of these recovered from the involvement of the bulbar musculature, and the diagnosis was made on clinical and biopsy considerations. The third patient had a subacute form that terminated fatally in 24 months. Autopsy showed severe muscular disease with connective tissue replacement and preservation of nerve fibers in the bulbar musculature, as well as in the skeletal muscle. The motor nuclei of the nervous system showed various states, ranging from normal to chronic neuron disease, but of such a degree that the process was interrupted as secondary. In the fourth patient the disease was acute and fatal in six weeks. The changes in the bulbar musculature were acutely degenerative, with edema, slight connective tissue reaction, no inflammatory reaction, and the preservation of nerve fibers. The spinal cord and brain had not yet been examined, but the vagus nerve, the brachial plexus, and the cauda equina showed no changes. These findings suggest that glossopharngeolaryngeal paralysis can occur in dermatomyositis as a result of peripheral involvement of the striated muscle.

The fifth patient had progressive muscular dystrophy. Autopsy showed severe dystrophic changes in the skeletal muscles and in the glossopharyngeolaryngeal area. There was preservation of nerve fibers in these muscles. The neuronal state varied from normal to some evidence of chronic ganglion cell disease, but of a degree interpreted as secondary. The conclusion that the paralysis of the bulbar musculature was also of peripheral origin appears valid.

The sixth patient had dystrophia myotonica with palatal weakness and dysphagia and the case was reported as clinical.

In the two cases in which the nervous system was examined at autopsy the neuronal disease was extensive throughout, not in the motor nuclei alone. It was recognized that in order to establish the hypothesis that this disease was not related to the cause of the muscular wasting, one would have to make cell counts on the anterior horns and motor nuclei of the brain stem, as well as fiber counts on the emerging axons. This is a project for future study.

DISCUSSION

DR. FREDERICK HILLER: It is not surprising that the bulbar muscles were involved. I should be interested in knowing whether the heart muscle was examined in any of these cases and, if so, what were the findings.

DR. WALTER R. KIRSCHBAUM: Little progress has been made in the understanding of dermatomyositis since the reports of Unverricht and others, about 1885. With the skin involved in 60% of cases, mere polymyositis, or myositis combined with disturbances of the mucous membranes, or of the vessels, or of peripheral nerves, was present in other cases. This variability led to the terms mucomyositis, myositis hemorrhagica, and neuromyositis respectively. The authors showed that in the present cases peripheral nerves were not involved and that the bulbar symptoms were the result of failure of vital muscular activities, as evidenced by the intensive degenerative process. They mentioned changes in the spinal cord. In two of their cases which I had the opportunity to study there were loss and degeneration of motor neuron cells and glial proliferations and glial stars in the white matter, findings which deserve a more detailed study, now in progress. The authors should be commended upon their broad view of the problem. Polymyositis is in reality a progressive degenerative myopathy, possibly due to metabolic-toxic agents, as in other, clinically different muscular dystrophies.

DR. HERMAN CHOR: I should like to ask Dr. Sherman two questions regarding the cases of dermatomyositis. Did the patients experience pain in the muscles, and were there muscles tender to palpation?

DR. R. M. STRONG: Did Dr. Sherman have an opportunity to make any observations on the condition of the collagenous fibers in the two patients with dermatomyositis who recovered? If he had such an opportunity, was there any evidence of regeneration of the skeletal muscle fibers?

DR. IRVING C. SHERMAN: I wish to thank Dr. Kirschbaum for reviewing the literature on dermatomyositis, which I could not include in the time allotted me. He said, however, that there were no cases in which the spinal cord was studied carefully. In one of the first cases described by Wagner, in 1887, careful neuropathologic studies were made. Since that time there have been no such reports. He noted that there was no change in the neurones.

Dr. Hiller stated that the involvement of the bulbar musculature is not surprising. I agree. However, the diagnosis is not always simple, especially when the bulbar signs are prominent. The third patient was examined in the ward at Cook County Hospital by at least four persons present here. One diagnosis was myasthenia gravis. Under Dr. Hassin's influence, I myself reported this case as one of ascending paralysis of Duchenne. Other diagnoses were peripheral neuropathy and progressive muscular atrophy.

In answer to Dr. Chor's question, the muscles were all tender. In the acute case the patient resisted palpation of the muscles. When the bulbar phenomenon comes on in a case like that, in which the diagnosis is obvious, there is no confusion.

Dr. Hiller asked about the heart muscle. In the three cases in which autopsy was done, two of dermatomyositis and one of muscular dystrophy, there was no change in the heart muscle.

Dr. Strong asked regarding the regeneration of the muscles in the cases of recovery. We had a hard time getting these patients to submit to biopsy while sick, and once they left the hospital it was difficult to get them back. I should be curious to see what the muscle looks like in patients who recover from this condition.

Dr. Walter R. Kirschbaum: To answer Dr. Strong's question, there was pronounced increase in endomysial connective tissue, which contains a considerable amount of collagenous tissue. The collagenous substance appeared to me not to be at fault, but I am unable to give an opinion as to whether or not dermatomyositis should be grouped with so-called diseases of the collagenous interstitial substances.

Vascular Lesions of the Central Nervous System Amenable to Surgical Treatment.

Dr. Robert C. Bassett (by invitation), Ann Arbor, Mich.

During the period 1941-1951 a total of 114 patients with intracranial aneurysm were seen. Sixty-six were treated surgically by one or more techniques. Of the surgically treated patients, 43 survived, a mortality rate of 35%.

Of seven untreated patients with aneurysm diagnosed by angiography who, for one reason or another, refused or did not receive the benefit of surgical treatment, three are dead and four are living. The four surviving untreated patients are asymptomatic and without evidence of deficiency of the central nervous system.

Thirty patients with cerebral angioma were seen during the same period. Of these, 25 were subjected to surgical management. Of this group, eight have died, seven of whom were treated surgically. Two of the seven deaths represent the operative mortality for the 25 surgically treated patients. Two other deaths occurred later, from recurrent hemorrhage, and the others from unrelated causes.

Fifteen cases of pial-medullary angiomas of the spinal cord have come to our attention. Fourteen of the patients were treated surgically. Five of these showed dramatic improvement with surgical treatment; five were not improved, and four were definitely made worse.

DISCUSSION

Dr. Oscar Sugar: Dr. Bassett and I have talked about this subject for some years. To operate on an aneurysm is a hazardous procedure, both for the surgeon and for the patient, and I shall not discuss that further. However, there is still lacking a good set of statistics on patients who have been treated conservatively over a long period. It would help in making decisions if one could say with some degree of assurance what would happen to the patients who were not treated surgically. Opinions expressed by various authors differ greatly. Dr. Bassett said the patient would die if he is not operated on. Dr. Mount has said the same thing. On the other hand, Hyland and others, in Canada, say that most patients will get along and that it is better to leave the lesion alone.

Dr. Paul Bucy: Dr. Bassett is to be congratulated on the courage with which he has presented many aspects. Many years ago we looked upon cases of brain tumor as one group. We have long since passed that point, and we now realize that we have to deal with each type of tumor and each location of tumor on its own ground, and that we cannot talk about them as a group. It is obvious from Dr. Bassett's presentation that we now must attack the vascular lesions in the same fashion. We have progressed from the period of some years ago, when

we looked upon these lesions as completely hopeless, as something that could not be attacked surgically. At that time we hoped that the patient would get better, but if not we could do nothing about it. That period has passed. But we must consider the type of attack for each kind of lesion. Should we leave it alone? Should we ligate the internal carotid artery? Should we merely ligate its principal blood supply? Should we remove the lesion? Should we coagulate it? These are all problems which are not yet completely answered, and will not be completely answered until we have accumulated groups of cases of every type and analyzed them carefully and compared our results. We are bound from time to time to go too far, and then we have to retreat and start over.

There was a time when certain surgeons, of whom Dr. Basset was not one, blindly and courageously attacked all these lesions directly. It is now recognized that that is not the optimum procedure for all lesions of this type. I do not think anyone is sufficiently familiar with this problem to state exactly what should be done in each situation. It is only by analyses such as this that we shall finally achieve our results, and they certainly need to be improved.

Dr. Roland P. Mackay: Dr. Bassett, in his excellent presentation, has discussed the various vascular anomalies as seen in the angiogram or at the operating table. For us who practice medical neurology the problem begins much earlier, in the matter of diagnosis and the selection of cases. When we first see the patient, we must make a diagnosis as to the type of vascular lesion which may be present, and, indeed, as to whether a vascular lesion is present at all.

Angiography is not an innocuous procedure in patients over 50 years of age, and probably not in those over 40. We must, therefore, first decide whether to have an angiogram. It would be well to know on what basis such a decision can be made. It occurs to me that a number of these lesions are arteriovenous malformations and that we might get a good deal of information if we could make simultaneous arterial and venous studies to determine whether the venous return is more arterial than it would be if the normal capillary bed lay between the two sides of the circulation.

Can Dr. Bassett tell us whether any such studies have been made in an attempt to arrive at a decision before the angiogram is made?

Dr. Robert C. Bassett, Ann Arbor, Mich.: In answer to Dr. Mackay's question, we have not done any physiologic studies on the circulation. Much of that work has been done at the University of Pennsylvania.

As Dr. Bucy indicated, the trend in most centers treating large numbers of aneurysms has been a return to the conservative approach. Reports of large series all emphasize more satisfactory results and a minimal mortality rate with simple cervical ligation of the internal carotid artery—in our series about 4%. This rate is spectacular when compared with the 35 to 40% mortality which haunts the direct intracranial approach to the problem. I believe all are agreed that we are as yet far from a satisfactory solution to the problem.

Gangliogliomas: Pathologic Study. Dr. Charles E. Corcoran.

The subject of nerve cell tumors of the central nervous system was briefly reviewed. It was pointed out that some of the presumed instances of nerve cell tumors in the study, selected on the basis of features claimed for the tumor group, had been erroneously interpreted. These tumors were considered gliomas containing adult nerve cells, and not tumor nerve cells, around which the tumor tissue had infiltrated in its growth.

The similarity in size, form, and staining between nerve cells in normal adult brains and the cells in tumors presumed to contain immature tumor nerve cells was shown. The belief was expressed that preexisting nerve cells, surrounded by the infiltrating tumor and so sectioned as to simulate immature forms, had been misinterpreted as embryonic or immature neural elements.

Certain facts of gross anatomy were pointed out to explain why in many reported cases, and in this study, these growths have been found so frequently in certain locations of the brain.

DISCUSSION

Dr. Ben W. Lichtenstein: I studied and reported a case of ganglioneuroma of the spinal cord, and I am confident that such a tumor exists in the central nervous system and that the ganglion cells do not represent inclusions of the normal gray substance. Dr. Corcoran has

reported his analysis of tumor sections from the collection of the Mayo Clinic and has stated his opinion concerning the presence of nerve cells in gliomas. He must remember that there is a great difference of opinion in tumor diagnosis and that his impressions may not be subscribed to by others.

Hugh T. Carmichael, M.D., *President, in the Chair*
Regular Meeting, Nov. 11, 1952

Multiple Sclerosis: Its Onset and Duration; A Clinical Study of Three Hundred Nine Private Patients. DR. ROLAND P. MACKAY.

In a survey of 309 private office patients, all of necessity ambulatory, the mean age of onset was 30.2 years and the median age 28.9. This finding is in approximate agreement with that of other authors. Careful inquiry is necessary to elicit a history of early, and often long-disregarded, episodes at the onset of the disease. Of the 309 patients, 136 were males and 173 females. The preponderance of females is probably fortuitous and does not represent a significant differential incidence. Nearly 30% of the patients were observed until they had lived more than 10 years after the onset of the disease. About 6.5% were still living after 20 years. These figures would certainly be greater if longer observations were possible.

It would appear that the so-called paraplegic type of mutiple sclerosis has a longer life expectancy and that the early involvement of the cerebellum carries an ominous prognostic significance. A truly "progressive" form of multiple sclerosis seems to be extremely rare. Remissions practically always occur early in the history and are only relatively less striking when superimposed upon enduring changes. The duration of life in multiple sclerosis is considerably greater than is commonly supposed, the mean duration being probably 20 years or more.

Critical Evaluation of Surgical and Medical Treatment of Vertigo and Ménière's Disease. DR. ROBERT B. LEWY (by invitation).

Vertigo is a false sense of motion or position in space. It is not to be confused with dizziness, which is a general term with many meanings, including neurologic uncertainty. Ménière's disease comprises a triad of vertigo, tinnitus, and deafness. There are many medical and surgical means of treatment. Of these, the most desirable is medical treatment, with use of a low-salt, low-fluid diet and, if medication be given, 50-mg. doses of pyridoxine. The last therapy is empirical. Surgical treatment must be restricted to cases in which chronic invalidism is threatened and the need is so great that hearing may be lost, if it is not already largely destroyed.

The essential pathologic process is located mostly in the end-organ, the labyrinth. However, since destruction of the labyrinth does not necessarily abolish tinnitus, it is probable that, in addition to the hydropic labyrinth, there is a state corresponding to causalgia, which may be represented in higher centers. This may be a dysfunctional condition, comparable in an intercellular sense to inflammation.

Blocking of the stellate ganglion and interruption of the cervicodorsal anterior gray rami offer a field for further research and an opportunity to control this condition without destructive surgery.

DISCUSSION

DR. BENJAMIN BOSHES: As I recall, this disease, as Ménière described it in his original article, was an acute hemorrhage into the labyrinth with destruction. Such an irreversible condition is quite different from what Dr. Lewy has described. Out of Ménière's original description has come a group of symptom complexes which some call Ménière's disease, or Ménière's syndrome. The difficulty arises because three symptoms are taken together and called a disease.

As I recall Dr. Walter Dandy's article, what he frequently found at operation were large blood vessels implicating the auditory nerve. To treat such a process by desensitization is futile. It is a little dangerous to designate therapy in a condition which is not a nosologic entity, but only three signs. One needs more reliable criteria than have been set up on the basis of a therapeutic result.

DR. ROBERT B. LEWY: The work of Passe and Seymour in blocking the stellate ganglion was done as a criterion of decision. If the stellate block abolished the vertigo, then sympathec-

tomy would presumably give permanent relief. They did not find, and I am quite sure that others will have the same experience, that the stellate block solved the problem in all cases.

I agree with Dr. Boshes that this condition may well not be a disease as such. However, in the opening paragraph of the paper I specified exactly what I meant when I spoke of Ménière's disease. If we all understand what we are talking about, both speaker and listener, I think the purposes of language and communication are being properly served.

I do not believe that anyone longer accepts Dandy's interpretation that arterial loops along the eighth nerve are responsible for tinnitus in most cases. As I have indicated in this paper, hydrops of the labyrinth was proved histologically in 16 cases of vertigo. Ménière in his original work, as analyzed by Miles Atkinson, really indicated that the hemorrhage in the labyrinth in Ménière's disease was purely coincidental. We no longer believe that this is the responsible pathology.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Harold G. Wolff, M.D., *President, New York Neurological Society, Presiding*
Joint Meeting, Feb. 19, 1952

Pentylenetetrazole (Metrazol®) Activation of the Electroencephalogram in Psychiatric Patients. Dr. Albert N. Browne-Mayers and Dr. Leonard R. Straub.

Two groups of psychiatric patients were studied with pentylenetetrazole: the first, those who on admission to the Payne Whitney Clinic manifested mildly to moderately abnormal changes in the brain waves in the absence of neurologic disease, previous electric shock, or insulin therapy; the second, those whose predominant complaints centered around disturbances in perception of self or the environment or who had acute rage reactions. These patients were called "epileptoid." The authors found that both groups of patients were more sensitive to pentylenetetrazole, injected intravenously at a rate of 20 mg. every 30 seconds for a total of 400 mg., than psychiatric patients who showed neither of the above abnormalities. Of the 26 control patients, 24 showed no further electroencephalographic changes when given pentylenetetrazole, and 2 showed moderately abnormal responses to the drug. Of the 13 patients tested because of electroencephalographic disturbances, 2 showed no further changes with pentylenetetrazole, 5 showed moderately abnormal responses, and 6 showed epileptiform wave patterns. Twelve patients were tested because of "epileptoid" psychopathological features, and 4 of these exhibited no further change with pentylenetetrazole, while 2 showed moderately abnormal responses and 6 epileptiform discharge. There was no epileptiform discharge in the control group. Of those with electroencephalographic abnormalities, six showed epileptiform wave patterns, and two of these had a grand mal seizure. Of the six patients in the "epileptoid" group who had epileptiform discharge with pentylenetetrazole, one had a grand mal seizure.

The authors believe that pentylenetetrazole is a sensitive tool for the evaluation of abnormalities in the brain waves in psychiatric patients. Although other workers have attributed electroencephalographic abnormalities to one or another psychiatric entity, the authors show that abnormalities were found in patients in many psychiatric diagnostic categories. Pentylenetetrazole proved useful in substantiating the diagnosis of epilepsy in one patient. This work points to the need for a broader understanding of electroencephalographic abnormalities in psychiatric patients.

DISCUSSION

Dr. Oskar Diethelm: I was surprised at how high the number of electroencephalographic changes was in routine admissions to our psychiatric hospital, but also at how low it was as compared with what we should expect from statements in the literature. It is obvious we cannot tie it in with nosological psychiatric entities but have to determine in which types of psychopathological reactions electroencephalographic changes occur. The observations which were presented speak for themselves. They offer a challenge and open a new path for investigation.

Dr. Harold G. Wolff: I should like to ask in what general direction they will lead us.

Dr. Leonard R. Straub: We have been particularly interested in the epileptoid group, and we hope by obtaining more patients of this type that may be able to clarify some of the

confusion in the literature. For example, in many diagnostic categories one finds reports to the effect that this or that clinical entity shows more electroencephalographic abnormalities than the other. A definition is the first step, and from there one should pursue other studies, perhaps in the way of photic stimulation.

DR. PETER G. DENKER: Since in so many of the cases described the condition resembled the "temporal lobe" type of seizures, I wonder whether the authors attempted to take sleep records to localize lesions in this area. Electroencephalographic changes often do not appear in the waking state in cases of temporal lobe epilepsy.

DR. LEONARD R. STRAUB: No, we have not made sleep records on these patients routinely; I think we should perhaps include them in the study.

Lesions of the Central Nervous System in Disseminated Lupus Erythematosus. DR. GILBERT H. GLASER.

This paper was published in full in the June 1952 issue of the ARCHIVES, page 745.

DISCUSSION

DR. LEWIS D. STEVENSON: This subject has interested us very much at the Bellevue and New York Hospitals. First of all, cases of lupus erythematosus are much more numerous in recent years; we have a number in both hospitals, but in only three did we find such lesions in the nervous system or any other significant lesions of the type Dr. Glaser has illustrated.

DR. HAROLD G. WOLFF: In your own cases, Dr. Glaser, were there symptoms referable to the central nervous system, such as papilledema?

DR. GILBERT H. GLASER: We did see symptoms of involvement of the central nervous system in a patient who had generalized seizures. The "papilledema" was regarded as due to a local retinal lesion, occurring in the absence of increased cerebrospinal fluid pressure.

DR. HAROLD G. WOLFF: Despite these dramatic changes, the signs visible at the bedside have been relatively minor?

DR. GILBERT H. GLASER: In this very small series, yes; however, a review of the literature indicates that a great variety of neurologic signs and symptoms, such as hemiparesis, focal and generalized seizures, and aphasia, can occur in the course of lupus.

Local Electrocortical Responses Induced by Topical Application of Acetylcholine Chloride to the Human Cerebral Cortex. DR. JOSEPH G. CHUSID and DR. C. G. DE GUTIERREZ-MAHONEY.

When 10 or 20% acetylcholine chloride solution was applied topically to the exposed cortex of 12 patients undergoing cerebral operations, profound changes in the local electrocorticogram occurred in 8 of the 29 test sites. Local early pronounced depression of electrical activity soon after the application of the acetylcholine chloride solution was not noted. There was usually a period of latency of six to eight minutes before significant electrocortical changes could be detected. Initially, recurrent single negative waves of increasing amplitude with a maximum of approximately 600 mv, a frequency of 1 to 2 cps and a duration of 0.2 to 0.3 second occurred. Thereafter, groups, clusters, or spindles of increasing duration, in which high-amplitude, 5- to 10-cps waves were dominant, were associated with the single high-amplitude negative waves initially noted. In the ensuing phase, the initial high-amplitude negative wave components were sometimes modified by abrupt positive deflections, so as to give the appearance of diphasic or triphasic spikes. After the maximum response, the bursts of groups, clusters, or spindles became less prominent, decreasing gradually in duration and amplitude; thereafter the initial high-amplitude negative waves and the spikes also disappeared.

When a pledget with 10% acteylcholine chloride solution was applied for one minute to a previously strychninized cortical site, a pronounced facilitatory effect was noted. Spike discharges immediately became more frequent and prominent and about 1½ minutes later became associated with spindle bursts of high-amplitude 8- to 10-cps waves. This response reached its maximum three minutes after the acetylcholine chloride was applied and rapidly diminished in the following one-half minute, the spindle bursts disappearing first. When a

previously responsive cortical site was retested soon after it had returned to its pretest pattern, a greatly decreased latency in the onset of the new response sometimes occurred. Preoperative medication, anesthesia, cerebral pathologic changes, leptomeningeal permeability, drug concentration, and duration and site of application were considered as possible factors influencing the results of this study.

DISCUSSION

DR. H. HOUSTON MERRITT: The work of Dr. Chusid and Dr. Mahoney is of great interest. It is, as far as I know, the first report of the direct application of acetylcholine to the human cerebral cortex. A great deal of work has been done in animals since the first reports by Dr. Charles Brenner and Dr. H. Houston Merritt, in 1942. The results obtained by Dr. Chusid and Dr. Mahoney in humans are quite similar to those in experimental animals.

The interest in the results of the application of acetylcholine to the cerebral cortex lies in the fact that there may be some connection between a disturbance in acetylcholine metabolism and epilepsy. All the evidence in support of this possible relation is indirect. It is therefore of great importance that the action of acetylcholine on the human nervous system be studied thoroughly.

Intracranial Circulatory Complications of Injuries to the Neck. DR. GEORGE H. HYSLOP.

Four cases illustrating apparent intracranial circulatory reaction to trauma to the neck were presented.

One patient had with reasonable certainty a thrombosis of the basilar and right posterior cerebral arteries initiated by extreme rotation of the head and pressure applied to the left side of the neck. Within four months there was recovery except for left upper quadrant homonymous hemianopsia.

The second patient had a very similar syndrome appearing within a few hours after a high neck sprain.

The third patient sustained a dislocation of the seventh cervical vertebra during sudden full lateral flexion of the head to the left and within a few moments had a short period of unconsciousness, followed by transient blindness.

The fourth patient, representing a different situation, had the signs of traumatic myositis and radiculitis of the right lower cervical region and over a period of four years has been subject to syncopal and epileptiform attacks which are correlated with neck and shoulder pain, frequently precipitated by motion of the right upper extremity at the shoulder joint.

The anatomic and physiologic factors were briefly discussed.

DISCUSSION

DR. I. J. SANDS: Has Dr. Hyslop had any cases of fracture of cervical vertebrae in which these phenomena also occurred?

DR. GEORGE H. HYSLOP: No, I have not seen this situation in cases of vertebral fracture.

DR. HAROLD G. WOLFF: Was there something special about the treatment of these cases, the way in which it was done—could you find anything which was peculiar?

DR. GEORGE H. HYSLOP: The first patient had the head extremely rotated to the left and pressure applied—I do not know exactly where. During the period of that position, or shortly afterward, the symptoms developed; the first were visual in nature, e. g., flickering and bitemporal scotomas. The second patient had a neck sprain with visual symptoms first, symptoms of lower cranial nerve involvement second, and, as in the first case, protracted mental change. The first patient had a quadrant homonymous hemianopsia. Each patient had in connection with the sprain of the higher part of the neck, either a compression or a stretching of the third or fourth part of one of the vertebral arteries by adjacent muscles. The third patient presumably had a pull on the right carotid artery. In each case there was an acutely applied mechanical force.

DR. LOUIS HAUSMAN: What did examination of the carotid sinus show in these patients?

DR. GEORGE H. HYSLOP: In the second and fourth patients, particularly the latter, there was clinically a tender carotid sinus.

DR. HENRY ALSOP RILEY: I believe that thrombosis of the basilar artery is an extremely serious condition and that it usually produces a much more serious disturbance than these transient symptoms—in the majority of instances death. I believe that the condition here is not a thrombosis of the basilar or vertebral artery, but is due to some irritation of the periarterial sympathetic plexus in relation with the vertebral artery.

DR. PETER G. DENKER: I should like to hear more about the first patient; did she have migraine for some years before the manipulation?

DR. GEORGE H. HYSLOP: Yes.

DR. PETER G. DENKER: I wonder whether she might not have had an aneurysm, which is occasionally present in people with long-standing migraine, and which might have been aggravated by the trauma.

DR. HAROLD G. WOLFF: Some people with migraine do have permanent vascular defects after an attack.

DR. I. J. SANDS: This paper deserves a good deal of discussion. In my experience, people who have sustained injuries to the neck fall into two groups: (1) those who have a definite fracture of a cervical vertebra (these patients do not present complaints of the type described by Dr. Hyslop), and (2) those who have sustained injuries while riding in taxicabs or automobiles and who have had a turning or twisting of the head and stretching of the neck. These patients have had complaints of the type described by Dr. Hyslop. The three upper cervical sensory nerves supply the posterior fossa of the skull and its contents. Moreover, traction or sudden twisting of the neck may cause injury to the autonomic nerve chains in the neck. Perhaps some such injury may be responsible for some of the symptoms described by Dr. Hyslop.

H. Houston Merritt, M.D., *Chairman, Section of Neurology and Psychiatry, Presiding*

Joint Meeting, March 11, 1952

Cysts of Sacral Nerve Roots: Pathogenesis and Clinical Significance. DR. I. M. TARLOV.

Since the author's discovery of sacral perineurial cysts at autopsy in 1937 and his demonstration of their clinical significance in 1948, nine clinical cases have been reported. All the cysts occurred under the posterior arch of the sacrum.

The development of slowly progressive changes referable to the sacral or coccygeal portion of the cauda equina should lead one to suspect such a cyst. It should be suspected also in a case of the sciatic syndrome in which operation fails to reveal a herniated intervertebral disk or other adequate cause of the patient's illness.

Experience with three cases in which were found transitional histologic stages between hemorrhages and cysts in the sacral ganglia has shown that hemorrhage may lead to cyst formation. The occurrence of thick-walled blood vessels surrounded by rarefied neural tissue, and even cavitation, strongly suggests that thrombosis and ischemia may also lead to cyst formation.

The finding of perineurial cysts on thoracic nerve roots in two cases suggests that these cysts may account for pain and associated symptoms and signs at other spinal, and possibly cranial, levels.

DISCUSSION

DR. ABRAHAM KAPLAN: Dr. Tarlov's concept of these cysts is that they are separate from the arachnoid space. I should like to ask, first, why he found these cysts so frequently in the sacral area and, second, how he explains the presence of blood from intracranial hemorrhage in the cyst if it is totally separate from the subarachnoid space.

DR. FRITZ CRAMER: I should like to ask whether Dr. Tarlov thought these cysts might be the result of trauma. It seems to me that direct trauma might play a part in their formation, particularly since in some cases the cyst was suspected of being herniated nucleus pulposus.

DR. ALEXANDRA ADLER: The formation of cysts has sometimes been described in connection with the Arnold-Chiari syndrome; I wonder whether there was any indication of an Arnold-Chiari malformation in any of these cases.

DR. E. JEFFERSON BROWDER, Brooklyn: It might be mentioned that other evidence in support of the chronicity of these cysts is the finding of a hollowed-out area on the lateral aspect of the sacral canal, a bony bed for the cyst. I have had experience with two examples of this character; however, in neither was unroofing of the cyst of benefit. The technical procedures may have been inadequate; consequently, the results do not detract at all from the fine work Dr. Tarlov has done.

These changes in the bone are somewhat comparable to the bony finding in the distal phalanx of the finger when a glomus tumor has made a bed for itself.

DR. H. HOUSTON MERRITT: I should like to ask why the patient improves when the affected root and ganglion are removed. Is the cyst pressing on other nerve roots as well?

DR. I. M. TARLOV: In answer to Dr. Kaplan's questions, I think these cysts are present elsewhere; we have just not looked for them. It is difficult to dissect the ganglion of all the spinal nerve roots. I am doing that now, and already I have found perineurial cysts of the thoracic ganglia in two cases. I am sure that more perineurial cysts of the thoracic and other ganglia will appear if we look for them.

Why is blood present in these cysts in association with intracerebral hemorrhage? The patients that had intracerebral hemorrhage also had subarachnoid hemorrhage, and my concept is that the subarachnoid hemorrhage, which was thick in the lower thecal space, distended the veins of the sacral ganglia and dorsal roots, causing their engorgement and rupture. The perineurial cyst resulted from this hemorrhage.

Dr. Cramer asked whether trauma can produce these cysts. I think it can; whether trauma per se causes the cyst or whether the mechanism operates through the production of hemorrhage is another matter.

Dr. Browder's comments are very interesting. Concerning erosion of the sacrum, Schreiber had two cases in which there was erosion of the posterior wall of the sacrum. The sacrum was "paper-thin." I wonder whether the fact that the entire cyst was not removed might not account for the failure to relieve the patient in Dr. Browder's first case.

Herpes Zoster with Muscular Involvement: Report of Three Cases. DR. I. S. FREIMAN and DR. P. LADERMAN, Jamaica, N. Y.

Three cases of herpes zoster with motor involvement were described. The first was characterized by dysfunction of the 5th, 7th, 9th, and 10th cranial nerves on the left side, with a herpetic eruption in the left external auditory canal. In the second there were an eruption and sensory impairment in the seventh cervical dermatome on the right, but pain and motor changes were more extensive, involving the sixth cervical to the first thoracic dermatomes in the right upper limb. In the third there were herpes and motor changes in the third lumbar segment of the left lower extremity. All cases were of the idiopathic type of herpes zoster, and ultimately considerable improvement occurred with only symptomatic therapy.

Reports of motor complication in herpes zoster have been accumulating, so that some authors consider motor symptoms an integral part of the disease. Pathologic studies have shown that involvement of the nervous system may be more extensive than the clinical findings suggest. Our cases and others recently reported indicate that motor involvement may be more extensive than sensory. All the evidence at present indicates that the virus of herpes zoster can attack the anterior and posterior roots, the sympathetic roots, the ventral and dorsal gray matter of the spinal cord or medulla, the meninges, and the peripheral nerves, in addition to the sensory spinal ganglia.

DISCUSSION

DR. HENRY ALSOP RILEY: I have seen at least three instances of herpes zoster associated with motor phenomena. Of these cases, two were very similar to those described by Dr. Freiman, but the third illustrates the possibility that the entire neuraxis may become involved in this postherpetic degenerative process, with the development of a generalized chronic poliomyelopathy.

DR. S. PHILIP GOODHART: The authors' report and discussion of three cases of motor symptoms associated with herpes zoster recall to mind a type of dyskinesia appearing during the epidemic of lethargic encephalitis of 1918-1919. I recall a number of cases in which we saw apparently radicular syndromes synchronously with or shortly after subjective sensory symptoms, together with motor reactions in the same area. The radicular pains were soon followed or accompanied by typical myoclonic movements in the same areas.

DR. I. S. WECHSLER: It is interesting to recall that herpes zoster at one time was called posterior poliomyelitis, in contrast to anterior poliomyelitis. I doubt whether the infection involves the roots primarily. The spread of the virus is to the cord itself, so that there is both an anterior horn, motor syndrome and a posterior, sensory syndrome.

DR. E. JEFFERSON BROWDER, Brooklyn: During my study of postherpetic neuralgia, material was collected which showed implication of the cord, dorsal roots, peripheral nerves, sympathetic ganglia, and skin in instances of herpes zoster. Dr. Laderman stated that the sympathetic roots were implicated. I should like to add that sympathetic ganglia as well may be extensively involved, particularly during the acute phase of the disease.

DR. ALEXANDRA ADLER: I should like to call attention to Oppenheim's "Diseases of the Nervous System" (Philadelphia, J. B. Lippincott & Co.), in which he speaks of some indication of muscular involvement in herpes; that was at least 50 years ago.

DR. MARY A. MARCUS: A prominent authority said that herpes simplex is due to a virus, but that herpes zoster is not. I wonder whether anyone knows definitely about this.

DR. H. HOUSTON MERRITT: This question needs clarification, for it is the common opinion that the virus for herpes zoster has not yet been isolated.

DR. I. S. FREIMAN: I believe there is no real proof of the nature of the virus, but there is plenty of evidence that there is a virus, and Dr. Landerman has summarized the evidence for it. There is recent evidence to indicate that herpes zoster may itself cause an encephalitis. It is plain that the lesion associated with true herpes zoster is an actual involvement of the skin by the virus, because the virus is recovered from the vesicles.

Clinical and Electroencephalographic Observations Following Prefrontal Lobotomy and Topectomy in Treatment of Chronic Psychoses. DR. ERICH G. KRUEGER and DR. HENRIETTE L. WAYNE.

The results of 85 prefrontal lobotomies and 20 topectomies in patients with chronic schizophrenia were reported. The rate of clinical improvement in the lobotomy group was considerably higher than that in the topectomy group. Lobotomy after ineffectual topectomy resulted in improvement of variable degree in five of seven patients.

The incidence of postoperative seizures was higher than is usually reported in other lobotomy or topectomy series. Possible factors for the higher seizure incidence were discussed. Whereas 15% of the patients had abnormal preoperative electroencephalograms, the majority retained abnormal tracings after operation. Topectomized patients showed somewhat less severe electroencephalographic changes, although they had in many instances marked slow-wave abnormalities in the anterior temporal area rather than in the frontal region. After operation barbiturates frequently did not elicit the usual acceleration of rhythm. Sleep spindle activity was more impaired after lobotomy than after topectomy.

The authors did not intend to convey the impression that fractional isolation or excision of the prefrontal cortex is generally ineffectual in the treatment of mental disorders. On the contrary, good clinical improvement, with reduction of undesirable side-effects, can be obtained in a variety of mental disorders of less severity.

DISCUSSION

DR. LOTHAR B. KALINOWSKY: I fully agree with the authors' conclusions. Those who saw the material presented could easily have been misled by the superiority of the lobotomy to the topectomy figures. This is obviously explained by the very chronic nature of the material. Disturbed chronic schizophrenics require a large operation, like the open lobotomy. I believe that any open operation, even if it is a lobotomy, increases the incidence of seizures. With the lobotomy, in order to avoid injury to vessels, the surgeon cuts a larger hole in the cortex than is done with a leucotome, in the blind operation; this makes inevitable a larger cortical scar and perhaps explains the higher percentage of seizures, though the seizures can always be easily controlled by proper medication.

DR. HOWARD P. KRIEGER: I should like to ask whether the authors had the opportunity to see whether a similar control group of patients who were treated with everything but psychosurgery would show about the same rate of recovery. Will the authors give their standards for judging recovery?

DR. FRANCIS ASBURY ECHLIN: A factor that perhaps is not considered very often in lobotomy or topectomy is the physiologic effect on the cells in the neighborhood of the lobotomy and at a distance.

DR. ERICH G. KRUEGER: We carried out this comparative study not only for its possible practical value, but also as a check on the validity of the working hypothesis of the Columbia-Greystone Associates (Mettler, F. A., Editor: Selective Partial Ablation of the Frontal Cortex: A Correlative Study on Its Effect on Human Psychotic Subjects, by the Columbia-Greystone Associates, New York, Paul B. Hoeber, Inc., 1949). This thesis originally implied that the removal of Area 9, or Area 10 as well, was the critical factor in lobotomy. Further studies on patients seemed to prove this point. The later experiences of Scoville's group (Scoville, W. B.; Wilk, E. K., and Pepe, A. J.: Selective Cortical Undercutting, *Am. J. Psychiat.* **107**:730, 1951) with undercutting of different areas appeared to disprove the first thesis. We felt that it was necessary to investigate whether the excision of one area alone was sufficient to achieve equally good clinical results under all circumstances and, if it was not, to prove the quantitative effect of psychosurgical procedures.

DR. HENRIETTE LOWENBERG WAYNE: We were working with very chronic material, mostly with a severely disturbed group of schizophrenic patients, for whom all other means of therapy had been exhausted. Whether the incidence of seizures is higher in the open type or in the closed type of lobotomy I am not prepared to say.

We did not use a control group because these patients were referred to us for the purpose of operation after every other means of treatment had been exhausted and we were to see what further results we could achieve in their rehabilitation. However, in a comparative study such as this, the lobotomy group serves as a control for the topectomy group.

DR. HAROLD G. WOLFF: Since these operations occasionally do help patients who are emotionally disturbed, is there any evidence to support the view that those patients who have fits do better than those who do not?

DR. HARRIETTE L. WAYNE: Not in our group. Stevens and Mosovich (Stevens, A., and Mosovich, A.: Clinical and EEG Investigation of Prefrontal Lobotomy Patients, *Am. J. Psychiat.* **104**:73, 1947), on the contrary, stated that poorer results occur in the patients who have convulsions than in those who do not.

Acute Respiratory Failure in Multiple Sclerosis and Its Management. DR. LOUIS BERLIN, DR. J. F. KURTZKE, and DR. T. C. GUTHRIE.

The manifestations of acute multiple sclerosis are often sudden in onset, but are also likely to subside rapidly and completely. Nevertheless, some patients die during an acute attack, even though that attack may not have been the first in the patient's history. It is probable that the fatalities in acute multiple sclerosis are attributable to ventilatory failure. This results from paralysis of the muscles of respiration produced by lesions of the cervical part of the cord. The incipient respiratory depression can be detected by noting the development of dyspnea, tachypnea, signs of rapidly progressive quadriparesis, and decreased vital capacity. Because of the tendency toward remission after acute attacks, it is probable that the deaths during the acute illness can be prevented by early treatment of the respiratory insufficiency. The only effective management rests in the use of a Drinker respirator.

Four patients with many episodes of acute multiple sclerosis manifested paresis of intercostal and diaphragmatic functions as part of an exacerbation of signs, which included quadriparesis. Two who were treated in the Drinker respirator improved and had only minimal residuals. The other two patients died during the acute episode, despite the use of oxygen by inhalation and tracheal aspiration.

DISCUSSION

DR. HAROLD G. WOLFF: May I emphasize that diseases as chronic as multiple sclerosis can often have explosive moments and that the vital-capacity apparatus is a necessary part of the neurologist's equipment? It is also extremely important to remember the possibility of respiratory failure in patients with myasthenia gravis and with the Guillain-Barré syndrome.

DR. H. HOUSTON MERRITT: Dr. Wolff's comment is worth bearing in mind. When I read the title of the paper, I was surprised that acute respiratory insufficiency was a significant

problem in multiple sclerosis, but when I recalled the deaths in the acute phase of the disease, I realized that they were due to respiratory insufficiency. I remember a recent patient who died in the respirator, possibly because he was not placed there soon enough. He died during the performance of tracheotomy to relieve excessive pharyngeal secretion.

DR. HAROLD G. WOLFF: Do the authors consider tracheotomy desirable to facilitate removal of secretions?

DR. LOUIS BERLIN: In the course of management of these patients, we have watched two of them with a good deal of trepidation, hoping we would not have to do a tracheotomy. In the past, whenever we felt we could get by with only endotracheal aspiration, we have hesitated to do a tracheotomy. We have had a recent case of chronic multiple sclerosis with an acute exacerbation in which there formed considerable secretion which could not be aspirated effectively; the patient had a tracheotomy; he still has a tracheotomy tube and is getting along relatively well. I think the safest thing is to perform a tracheotomy. If we fail to do it, we hope that we shall get by without too much aspiration.

Harold G. Wolff, M.D., *President, New York Neurological Society, Presiding*
Joint Meeting, May 13, 1952

Hepatic Dysfunction in Hepatolenticular Degeneration. DR. EDWARD C. FRANKLIN and DR. ARTHUR BAUMAN.

Eleven cases of hepatolenticular degeneration were studied to determine the incidence of clinical evidence of hepatic dysfunction. Symptoms and signs of liver disease were apparent in seven cases. In five of these cases hepatic symptoms preceded any neurogenic disorder by 2 to 14 years. In the other two cases hepatic failure occurred later in the course of illness. Laboratory tests of hepatic function gave abnormal findings in five of six cases with clinical signs of hepatic failure. Few liver function tests were performed in cases without clinical evidence of hepatic dysfunction. These tests confirmed the clinical impression of hepatic insufficiency but added little in the way of diagnosis. The duration of life ranged from 2 to 19 years, with nine patients living 9 or more years. We were unable to correlate the severity of liver disease with the course or the duration of illness. Of the 10 patients who died, hepatic failure was directly responsible for the death of 4. A complete necropsy was done in six cases, and only the brain was examined in a seventh. There was advanced multilobular cirrhosis in every case, and splenomegaly was present in five of the six cases. In every brain lesions characteristic of hepatolenticular degeneration were found. We feel that this evidence is confirming our impression that frank hepatic decompensation is commonly seen in hepatolenticular disease, a fact that has not been sufficiently emphasized.

DISCUSSION

DR. THEODORE J. C. VON STORCH: This paper brings up two points: 1. Perhaps if we look more carefully for neurologic disorder in patients with hepatic disease, we may occasionally find hepatolenticular degeneration earlier than we do. 2. A possible relation between neurologic and hepatic disease is suggested. Such a relation is coming to the fore at the present time, perhaps not in respect to hepatolenticular degeneration, but at least in connection with other extrapyramidal and pyramidal diseases.

DR. HAROLD G. WOLFF: I should like to ask whether the brain and liver are affected by a common toxic agent, or whether the defects in one organ are causally related to the other.

DR. DONALD J. SIMONS: I wonder whether the authors investigated the copper metabolism in any of their cases.

DR. ARTHUR BAUMAN: I cannot answer your question, Dr. Wolff. Wilson (Wilson, S. A. K.: Progressive Lenticular Degeneration, *Brain* **34**:295, 1912) postulated that the primary defect was hepatic. Barnes and Hurst (Barnes, S., and Hurst, E. W.: Hepato-Lenticular Degeneration, *Brain* **48**:279, 1925) supported this theory. These authors stated that the liver is probably injured by repeated bouts of hepatitis, either clinical or subclinical, presumably infectious. After sufficient hepatic damage, the liver cannot neutralize certain "toxins" which are capable of producing damage to the central nervous system.

DR. HAROLD G. WOLFF: Do your studies support this position?

DR. ARTHUR BAUMAN: As I stated, five of our patients had such extensive hepatic damage that signs of hepatic failure were the presenting symptom. However, the other six patients exhibited neurologic symptoms first. Although it is our impression that hepatic dysfunction frequently occurred first, we cannot logically conclude that hepatic damage is the cause of the damage to the nervous system. With regard to the etiology, we do not believe that the process is infectious; we think the cause is probably a metabolic defect. Abnormalities of copper and amino-acid metabolism may be operative as a cause of hepatolenticular degeneration or may coexist with another, as yet unknown, metabolic derangement.

As to the question about copper metabolism: Our last patient (Case 7) was transferred to the Hospital of the Rockefeller Institute for Medical Research, where Dr. A. Bearn showed that he had a relatively low serum copper level. After treatment with dimercaprol (BAL) the urinary excretion of copper was greatly increased. Dimercaprol failed to influence the patient's course significantly.

DR. H. HOUSTON MERRITT: Was this patient the one who died after your paper was written?

DR. ARTHUR BAUMAN: Yes, sir.

A Study of the Syndromes of Denial. DR. THOMAS C. GUTHRIE and DR. EUGENE M. GROSSMAN.

This paper was published in full in the September 1952, issue of the ARCHIVES, page 362.

DISCUSSION

DR. JAMES H. WALL: Dynamically, left sidedness is associated with homosexuality, which is often denied or projected. The mechanism of denial also plays a role in certain philosophies and religious beliefs.

DR. EDWIN A. WEINSTEIN: Dr. Guthrie and Dr. Grossman are to be congratulated on two excellently worked-up cases. They were most ingenious in their demonstration that in the presence of the organization of function, of which denial is a part, the patient will deny anything that he feels is seriously wrong with him. In the study of the premorbid personality such patients are usually found to be obsessional. Studies of this kind teach us a great deal about what happens in a prefrontal lobotomy. There one is concerned with the same kind of denial.

DR. THEODORE J. C. VON STORCH: If the theory that the syndrome of denial is determined by the premorbid personality is to be substantiated, the syndrome should occur more frequently with right-sided lesions and with lesions of other portions of the body unrelated to the central nervous system.

DR. THOMAS W. CARR: I should be interested in knowing how these patients deal with sensory stimuli on the left side of the body and whether the "draw-a-figure" test was performed on the patients who could see to determine how they depicted the other arm.

DR. BERGMAN: What was the nature of the speech disturbance; was it the peculiar method of referring to the left extremities, or something else?

DR. ABRAHAM M. RABINER, Brooklyn: Whether this syndrome is labeled anosognosia or self-denial, the structural basis for the disturbed function is localized in the contralateral cerebral hemisphere. In hemiplegia, even without evidences of associated hemisensory loss or impairment, the patient often does not appreciate a painful stimulus applied to the paretic limbs when similar stimuli are simultaneously applied bilaterally. Whether this phenomenon is called extinction or, as I believe, an impairment of attention, the underlying process seems similar to that of anosognosia.

DR. RICHARD M. BRICKNER: I believe it is risky to assume that in gross organic disturbances of the central nervous system many of the resulting symptoms are psychologically determined.

DR. H. O. PINEAS, Katonah, N. Y.: In 1926 I presented five cases of left hemiplegia. At that time I tried, without success, to localize the lesion. I compared these cases with other cases of left hemiplegia with loss of sensorium, but I concluded that one could not localize the phenomenon of anosognosia, and I raised the question whether the disorder might not be a personality problem.

DR. H. R. ROSENHECK: How does Anton's syndrome, in which there is persistent denial that complete blindness exists, fit into this concept, which has interested and intrigued us all?

DR. THOMAS C. GUTHRIE: We believe that the last patient presented Anton's syndrome and that this syndrome, as well as the others, is an additional example of the denial situation.

Cerebrospinal Rhinorrhea with Pituitary Tumors. DR. LUIGIA NORSA.

Cerebrospinal rhinorrhea has been reported as following trauma, both accidental and surgical; infections; congenital anomalies, and brain tumors.

Its association with pituitary tumors was brought to my attention by the case of a man aged 30 with a history of obesity and headaches of long standing, who after the onset of rhinorrhea had three recurrences of meningitis within three years. The patient died after craniotomy, undertaken for the repair of the cerebrospinal fluid leak; autopsy revealed a chromophobe adenoma eroding the sella turcica and infiltrating the leptomeninges.

Cerebrospinal rhinorrhea with pituitary tumors is uncommon, having been reported to date in only 7 pathologically verified cases, and on clinical grounds alone in about 20 additional instances. The condition, however, seems to be associated more frequently with pituitary neoplasms than with any other type of brain tumor.

While increased intracranial pressure of long standing, leading to erosion of the dura and, eventually, of bone, appears in general to be the common denominator in rhinorrhea associated with brain tumor, a single cause for the relative prevalence of rhinorrhea with pituitary neoplasms cannot be invoked; different factors, including coexisting defects about the cribriform plate and pressure necrosis of the sella turcica together with disruption of the subarachnoid space, seem to be involved in different cases.

DISCUSSION

DR. ABRAHAM KAPLAN: In 1929, while studying at Dr. Sachs's clinics, I had my first opportunity to see a case similar to Dr. Norsa's, in which the condition was unrecognized. The diagnosis was meningitis. There was no history of rhinorrhea. Autopsy, surprisingly, revealed a chromophobe adenoma of the pituitary, which had eroded the floor of the sella turcica into the sphenoid sinus, producing basilar meningitis. Unfortunately, pituitary tumors may on unusual occasions extend downward into the sphenoid sinus, producing suboccipital headaches, without ocular signs or evidence of pressure on the optic nerves. These tumors may also extend backward and laterally. In Dr. Norsa's case the unfortunate complication of bleeding was encountered. Had it not been for this complication, considerable tumor tissue could easily have been removed and the dural defect blocked off with absorbable gelatin sponge (gelfoam®) or muscle and a good surgical result thereby obtained.

DR. MORTON NATHANSON: Prior to operation was there roentgenologic evidence of spontaneous pneumocephalus?

DR. LUIGIA NORSA: There was no evidence of pneumocephalus at any time in my case.

Migraine Headache with Preheadache Retinal and Visual Disturbances in a Case of Congenital Vascular Anomaly and Subarachnoid Hemorrhage. DR. ARLINE CALDWELL and DR. RALPH KENNEDY.

A case of migraine and subarachnoid hemorrhage in a patient with an arteriovenous malformation was presented.

In 1944 the patient had the onset of left-sided scintillating scotomas, with episodic recurrences, and, beginning in 1945, associated left-sided numbness and paresthesias, and headache, which was usually left sided.

In 1946 the patient was hospitalized, after an episode of sudden loss of consciousness, lasting one hour, and was advised that he had had a cerebral hemorrhage, with bloody cerebrospinal fluid. After this he received 45 x-ray treatments to the right occipitoparietal area.

On his admission to the Veterans Administration Hospital, in 1952, x-ray studies revealed a linear calcification in the right parietal area near the midline. A right carotid arteriogram demonstrated an extensive arteriovenous malformation in the right posterior parietal area. The electroencephalogram revealed a slow-wave focus in the left anterior temporal area.

On one occasion, examination of the fundi at the onset of scotomas revealed slight generalized spasm of the retinal arterioles with intermittent marked segmental spasm. The headache was aborted by administration of 0.5 mg. of ergotamine tartrate.

The late onset of migrainous headaches and the absence of a familial history were probably significant of the presence of an associated intracerebral lesion.

The causal relation of the headache to the vascular anomaly was not clear, especially since headache rarely occurred on the same side as the aneurysm.

DISCUSSION

DR. HENRY ALSOP RILEY: Migraine can be a symptom of an underlying structural alteration in either the parenchyma or the vascular structures of the brain itself. This is well recognized. The unusual characteristics of this case would relate it to the symptomatic, rather than to the idiopathic, type of migraine. The part of the presentation which Dr. Kennedy did not stress is one on which I should like to have further elucidation, namely, the psychiatric aspects presented by the patient.

DR. H. HOUSTON MERRITT: Did you have cerebral angiograms of both sides? Sometimes vascular malformations are multiple.

DR. GEORGE H. HYSLOP: Statistical information might be helpful in the speculation about the association between true, or idiopathic, migraine and other recurrent headaches, which sometimes are caused by vascular lesions, anomalies, or of other nature.

DR. RALPH KENNEDY: Dr. Riley, I think I can best describe the patient as a passive-dependent person.

A left carotid arteriogram was attempted, but was unsuccessful.

Hemodynamic Patterns in Pressor Responses to Stressful Life Situations. DR. PHILIPPE V. CARDON JR.

The pressor response to stressful interviews was studied in 50 hypertensive patients with the aid of the Nickerson low-frequency ballistocardiograph. The object of the study was to evaluate the respective roles, in this response, of increased cardiac output and of vasoconstriction. In about two-thirds of the patients the rise in blood pressure was apparently due entirely to a rise in cardiac output. Such patients usually displayed overt evidence of emotional disturbance, such as blushing, crying, dry mouth, cold sweaty extremities, or freely expressed anger. In the remaining one-third, the cardiac output fell or remained constant; so the pressor response was apparently a result of vasoconstriction. These patients usually presented a smooth, unruffled exterior, their behavior being marked by evasiveness and sardonic humor. The same patient might display different patterns at different times, from day to day, or from minute to minute. The possible bearing of the type of hemodynamic response to stressful situations on the development of serious vascular disease was discussed.

DISCUSSION

DR. CHARLES ROSENHECK: Dr. Cardon is assuming that in most, if not all, of these cases, the response is neurogenic. Has he made comparable studies of the hemodynamics on clinically acceptable cases of organic hypertensive cardiovascular disease? One may postulate, cautiously perhaps, that in the neurogenic forms "physiologic" stress influences the dynamics and that in the hypertensive cardiovascular types one is confronted by a totally different type of stress, which one may, with equal caution, label "organic."

DR. PHILIPPE V. CARDON JR.: I am not entirely convinced of the difference between the neurogenic and the "organic" type. I think they are probably opposite poles of the same disease process. If I had to guess, I should say that in the so-called neurogenic type, in which the emotional component in the patient's illness is obviously great, the patient would react with the pattern of the high cardiac output I showed, whereas the patient in whom this element is not readily apparent, and is externalized only by prolonged psychiatric investigation, would present the second type.

Activation of Herpes Simplex by Section of the Trigeminal Nerve. DR. CHARLES A. CARTON.

In cases of trigeminal neuralgia in which sensory root section had been performed via the extradural subtemporal approach, the incidence of postoperative herpes simplex infection in the denervated areas was high, the typical homolateral eruption being present in 44 of 45 consecutive cases. It was postulated that these lesions were due to reactivation of herpes simplex virus

latent in the skin and mucous membranes of the lips, cheek, and palate, rather than to virus migration peripherally from the ganglion (Carton, C. A., and Kilbourne, E. D.: Activation of Latent Herpes Simplex by Trigeminal Sensory-Root Section, *New England J. Med.* **246**:172, 1952).

Injury to the Gasserian ganglion and preservation of the integrity of the neural pathway to the skin appear to be prerequisites for virus activation under these conditions. This was illustrated by the inability of alcohol injections or nerve avulsions distal to the ganglion to produce herpetic lesions, while sensory root section regularly resulted in such lesions. However, if the neural pathway had been destroyed, as shown in six cases in which alcohol injection, infraorbital nerve avulsion, mandibular nerve section, or prior partial sensory root section had been done, subsequent sensory root section did not result in herpetic lesions in the previously denervated areas.

On speculative grounds, trigeminal sensory root section was assumed to be a stimulatory phenomenon producing changes in the skin favorable to virus multiplication. Further elucidation of this mechanism of virus activation awaits a comparable test system in animals.

DISCUSSION

DR. HAROLD G. WOLFF: How often does herpes occur during attacks of trigeminal neuralgia? I have seen it occasionally, and I wonder whether Dr. Cardon has data on the incidence of herpes as an accompaniment of attacks.

DR. ABRAHAM KAPLAN: What is the explanation of the difference of herpes zoster which involves the first division, producing scarring with intractable pain, and the herpes following trigeminal section?

DR. CHARLES A. CARTON: As to Dr. Wolff's question, I do not believe we have any correlation between the cause of trigeminal neuralgia and that of herpes simplex. Certainly, we have found no herpetic eruptions during attacks.

In reply to Dr. Kaplan's question, I think that, although herpes zoster and herpes simplex are both caused by viruses, the eruption under discussion is primarily herpes simplex; it is interesting that we have never noticed herpes simplex in the first division of the nerve. Herpes zoster, which is usually limited to the ophthalmic division, is a problem which we did not study.

I did not mention that the virus studies in this project were performed by Dr. E. D. Kilbourne, formerly of the Rockefeller Institute for Medical Research and now of Tulane University of Louisiana, and by Dr. S. Ellison, of the Department of Bacteriology, Columbia University College of Physicians and Surgeons.

DR. HAROLD G. WOLFF: These experiments indicate that the host is harboring this organism for indefinite periods. Hence, changes in the host's state make it possible for the virus to damage tissue. These observations focus the interest of the investigator on the host, rather than on the parasite. This is an important indication of direction of thought in experimentation with micro-organisms.

Involvement of the Nervous System in Relapsing Uveitis with Recurrent Genital and Oral Ulcers (Behcet's Syndrome). DR. CHRISTIAN HERRMANN JR.

A white youth aged 17 with recurrent oral ulcers for two years, genital ulcers for one year, and uveitis for seven months, had onset of general weakness, drowsiness, unsteadiness of the hands, and drunken gait two months before admission. He also had recurrent swelling of joints, pimples and boils, epididymitis, and external otitis.

A low-grade fever, soft aortic systolic murmur, palpable liver, bilateral cerebellar signs, left third nerve paralysis, right sixth nerve paralysis, nystagmus, severe visual impairment, mild euphoria, and mild intellectual deterioration were noted. The spinal fluid had an initial pressure of 220 mm., with 115 cells per cubic millimeter (75% polymorphonuclear leucocytes and 25% lymphocytes). The protein was 68 mg. per 100 cc. and sugar 66 mg. per 100 cc. The Kolmer reaction was negative, and cultures were sterile. The electroencephalogram was diffusely abnormal. The sedimentation rate was elevated, with slight increase in prothrombin time.

Antibiotics, chemotherapy, and administration of cortisone and corticotropin did not alter his course. The spinal fluid returned to normal, but severe cerebellar deficit remained, along with blindness and glaucoma on the right and vision limited to light perception on the left.

DISCUSSION

DR. LAWRENCE H. GAHAGAN: What was the patient's racial background?

DR. CHRISTIAN HERRMANN: His father was born in Italy, and his mother was American-born, of Italian extraction.

DR. H. HOUSTON MERRITT: In what percentage of the total number of cases did signs of involvement of the nervous system develop?

DR. CHRISTIAN HERRMANN: In 9 of 40 patients, or 22.5%, I might add that only with involvement of the central nervous system has death occurred in these patients, and the duration of the disease may be up to 19 years.

Electrocardiographic Changes Produced by Head Trauma in Mice. DR. SHERWOOD A. JACOBSON and DR. PHILIP DANUFSKY, Brooklyn.

Albino Swiss mice were struck once on the top of the head while continuous electrocardiograms were being taken. The mice had been anesthetized with intraperitoneal injections of thiopental, and a series of nine were traumatized without and six with preliminary intraperitoneal administration of atropine. To determine the effects of pure anoxia, the tracheas of five anesthetized mice were exposed and clamped while electrocardiograms were being taken.

Analysis of the records showed bradycardia, changes in the amplitude of the P and T waves, and abnormal arrhythmias appearing in the group with head trauma without atropine at a statistically significantly greater frequency and earlier appearances. In the groups with head trauma there were changes in the amplitude of the QRS complex that were not effected by the administration of atropine, and that were not produced by anoxia as early as by trauma.

From these data is was concluded that damage to the intracranial contents can produce changes in the electrocardiogram identical with those produced by vagal stimulation, as well as changes in the QRS complex that were not effected by the use of atropine. There was also noted more changes in the T waves than had been reported as the result of vagal stimulation, and these changes were prevented by atropine.

The authors found abnormalities of rate and rhythm in brain-damaged patients roughly similar to those found in the brain-damaged mice.

DISCUSSION

DR. THOMAS C. GUTHRIE: How long after these fatal injuries did all electrical activity in the heart cease?

DR. SHERWOOD A. JACOBSON: From about 10 minutes to over one hour.

DR. MURRAY BORNSTEIN: It has been demonstrated that acetylcholine in minimal concentration, up to 10 γ per 100 cc., may be demonstrated in the cerebrospinal fluid of animals subjected to head trauma. Acetylcholine has also been found in patients who have had injuries to the head. The electroencephalographic and clinical changes in these animals may be reversed by atropine, and I wonder whether the possibility that the administered atropine may be acting in the central nervous system has been considered in the present experiments.

DR. SHERWOOD A. JACOBSON: We feel it was not a humoral agent, as has been presented previously in the literature, because most of the changes that were significant appeared within 0.5 second, some of them within 0.3 second. This rapid onset indicates nervous, rather than humoral, activity.

PHILADELPHIA PSYCHIATRIC SOCIETY

Hugo Mella, M.D., *President, in the Chair*
Regular Meeting, Oct. 10, 1952

Group Psychotherapy with Institutionalized Senile Women: Studies in Gerontologic Human Relations. DR. MAURICE E. LINDEN, Norristown, Pa.

The typical public mental hospital of today has about a 36% admission incidence of persons over 65 years of age. Over a third of the inpatient load consists of chronologically senile persons. But very little of the main therapeutic effort is directed toward this group, for a

variety of reasons, among them, lack of challenge, apparent hopelessness, and imminent death. A simple program of custodial care of the senile hospital population yields improvement in 5 to 10%. Any additional variety of environmental manipulation promises a greater rate of social improvement.

On the premise that senility is not a biologic stage of the human organism but is, rather, a product of cultural attitudes, it is seen that the senile person manifests psychologic needs intrinsic to his station in life. Senility should not be regarded as second childhood. It is childhood in reverse. This implies a subtle difference in the management of the pathologically aged and the treatment of children. Transference phenomena are seen in the aged. The senile ego still possesses traces of adult sexuality. The senile person retains vestiges of a former reasoning, judicious, and responsible ego.

The special areas of the therapeutic needs of senility are dependency, isolation, psychophysiologic exhaustion, phantasy formation, regression, empathy, and identification. In pathologic later maturity the person is both a prototype of senility and a caricature of himself. His twofold requirements can be managed in the process of group psychotherapy.

The criteria for selection of patients in the formation of a senile group, the setting for group development, group taboos, and the nature of group leadership were discussed. Some of the events and samples of conversation experienced in the process of group solidification were recorded.

Statistical examination of a group of 51 women selected from among 330 living in the same building and given group psychotherapy over a period of two years revealed social improvement, either moderate or marked, in 59%. Forty-five per cent of the group were released, or were able to be released, to nearly full social capacity, while only 13% of the patients not receiving group therapy were released during the same period. There was no significant relation of the type of participation (active or passive) to the response to therapy. The best results were obtained with senile patients, women with cerebral arteriosclerosis or late involutional depressions, and postlobotomy patients. Incontinence improved greatly with group therapy. Group work assisted in the resolution of depressive affects, increased alertness, diminished confusion, improved orientation, and replenished many memory hiatuses, all being reflected in bettering of the many minute factors inherent in ward socialization.

Group Psychotherapy with Male Stutterers. Dr. Morris W. Brody and Dr. Saul I. Harrison.

A group of male stutterers were given psychoanalytic group therapy. They presented dramatic transference phenomena. They banded together cohesively against the therapist, claiming that he could not understand because he did not stutter. This difficult transference situation was utilized to formulate interpretations. As therapeutic progress was achieved, insights were gained in group dynamics and the psychodynamics of the male stutterer.

The primary problem of the individual in this group was excessive superego demands with obsessive-compulsive characteristics. The stutterer considers himself to be an incomplete person and struggles against his defect. Speech was of vital importance to these patients. This overevaluation resembled the attitude usually found toward the phallus. For the stutterer speech is not primarily propositional. It is a means of expressing emotions, and the stuttering represents the expression of, the defense against, and the punishment for, the forbidden affects. Stuttering is a psychosomatic disorder, and the stutterer has regressed to an oral-respiratory level. The role of respiration was discussed.

Comments were offered on the relative merits of symptomatically homogeneous and symptomatically heterogeneous groups. Resistance, transference, countertransference, and their handling were discussed in detail. This method was compared with the psychoanalytic therapy of an individual.

DISCUSSION ON GROUP PSYCHOTHERAPY PAPERS

Dr. Louis Wender, New York: I had the good fortune to read Dr. Linden's paper before this meeting. It is convincing and stimulating. His ideas fit in logically with the purpose of group psychotherapy, with present reference to the weak, insecure, rejected person who feels lost and begins to flounder. This is part of present-day living.

Group psychotherapy deals with traumatization in early childhood, and it is apparent that it should be of benefit in the treatment of patients who are in childhood in reverse, namely, senile patients.

Group psychotherapy should be practiced in all the wards of a hospital where the patients are not violently disturbed or deteriorated. One is apt to neglect the patient after his acute psychotic episode has subsided and the psychosis remains dormant. The patient then becomes idle; he has no drive and no interests. A small percentage are given employment or occupational therapy, but in the large mental hospitals the percentage of these people who do some work is at a minimum. They feel that they belong because the ward physician and the ward nurse become their good father and mother, who in a kind way allow them to express themselves, for good or bad, without punishment.

I am of the opinion that occupational therapy is a component of group psychotherapy. Group psychotherapy in a hospital environment does not stop with the group psychotherapy sessions. It permits the patients in the ward to become more friendly, more intimate, although they may argue once in a while, this is on a friendly basis. In my early connections with Hillside Hospital, at Bellerose, N. Y., I organized groups in the individual cottages. It would have been impossible to do this if there had been no group psychotherapy. I have carried this plan forward at my sanitarium at Pinewood. All members of the group psychotherapy class, who are in one building, are admitted to the Pinewood Club. They meet once a week. Of course, at group psychotherapy sessions, gripes are not discussed except in rare instances, and then only for interpretive reasons. This gives them an opportunity for self-expression, a feeling of not being isolated. It gradually permits them to express their aggression, which they were fearful of doing prior to hospitalization. It gives them a feeling of worth, of doing something.

One can appreciate Dr. Linden's enthusiasm about his results, for he has seen changes in the senile patients who are not demented, who find a new avenue of expression, and who, after being rejected, isolated, and forgotten, have learned that they can still express themselves, obtain recognition, and that someone, a father image, cares for them. Dr. Linden is to be congratulated on his efforts, and I hope that he will continue in this masterly undertaking in group psychotherapy with senile patients, although one may not accept all his concepts on the psychological approach to senility.

Dr. Samuel B. Hadden: Second childhood is to many a devastating experience. Dr. Linden's courage and zeal in following out this program are worthy of our congratulations. He acknowledged that as a result of his group experience he had grown in stature; I am sure this is the experience of everyone who has ever attempted group psychotherapy.

The addition of an ancillary therapist improved the group. The presence of a mother figure eases group anxiety by counteracting the punishing father figure. I hoped to hear Dr. Linden say that with a dual therapist things went better. They usually do, especially with one of the sex opposite that of the therapist.

I believe that Dr. Harrison and Dr. Brody had the trouble of dealing with their countertransferences. Dr. Harrison said that when the sessions remained at the level of symptom discussions for a long time there was a feeling of discouragement in the group and they (the therapists) felt that they were isolated; I think that this was countertransference and that they felt the need of defending themselves. I have felt that after the group gets beyond the level of symptom discussion, invariably the patients will begin to speak of their feelings of inferiority. At this point it is well to try to divert the discussion from the symptom toward the genesis of their feelings of inferiority. Then they will get to a discussion of their feelings of parent relationship. They are prone to follow certain courses, and I have felt recently that, with their shifting transference, inevitably the individual becomes aware of the therapist at the start as a father figure and that the therapist remains a father figure for a long time, regardless of the sex of the group; but with male groups I have become not so much a father figure as a devil's advocate—a parent figure of the opposite sex; for instance, one member of the group will say, "Mom, what have you got to say?"

Obituaries

CLARENCE H. BELLINGER, M.D.
1887-1952

Dr. Clarence H. Bellinger, senior director of the Brooklyn State Hospital, and one of the most progressive psychiatric administrators, died Aug. 12, 1952, at the age of 65.

Dr. Bellinger was born in Lebanon, N. Y., on Feb. 12, 1887. He received his medical degree at the University of Syracuse in 1910. For the next 42 years he was associated with the Department of Mental Hygiene of the State of New York and in 1935 was appointed director of the Brooklyn State Hospital. At that time this hospital was a relatively small one, but, with his accustomed vigor and forcefulness, he managed in a short time to equip a long-idle multistoried building, so that the patient population was practically doubled within a year of his appointment.

Although primarily an administrator, Dr. Bellinger encouraged scientific interest and research as an intimate part of the treatment program for his patients. He emphasized that his hospital was truly that—a hospital for treatment, and not a custodial institution. He was one of the pioneers in the use of various forms of shock therapy and organized one of the largest centers for group therapy in a mental institution. Perhaps his greatest contribution to hospital psychiatry was the encouragement he gave to volunteer groups, and the incorporation of such groups into the broad therapeutic program of the hospital. In a similar manner, he encouraged the formation of independent clinics for outpatient treatment in various areas in the city of Brooklyn. These clinics were staffed by men from his own hospital and became part and parcel of a relatively vast program for community health.

He was indeed an unusual person, and his name will long be remembered for the many monuments he made in the field of mental health.

C. F. Terrence, M.D.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Meninges and Blood Vessels

KLEBSIELLA PNEUMONIAE MENINGITIS. J. THOMPSON, B. WILLIAMS, D. WILLIAMS, and M. ANDERSON, A. M. A. Arch. Int. Med. **89**:405 (March) 1952.

Meningitis due to Klebsiella pneumoniae (Friedländer's bacillus) is one of the less common forms of meningeal infection. In this communication 118 cases, including 31 with recovery, gathered from the world's literature to date are reviewed. An additional case, with bacteremia and pneumonia, and with recovery on penicillin, aureomycin, and streptomycin therapy is presented

Thompson and his colleagues report that the most frequent K. pneumoniae infections associated with meningitis are those of the ears, the upper and the lower respiratory tract, and wounds. In infants the primary focus is most frequently undetermined.

It was found that diabetes mellitus is associated with K. pneumoniae infections beyond its expected occurrence in random population groups. The presence of glycosuria and ketosis during the acute stages of the disease, however, does not necessarily indicate true diabetes mellitus.

The authors found no definitive clinical characteristics distinguishable from those of other forms of purulent meningitis to be evident. A gelatinous spinal fluid sometimes occurs. Petechiae have been noted. Streptomycin, aureomycin, chloramphenicol, and oxytetracycline (terramycin) all exert an antibacterial effect upon most strains of K. pneumoniae. Which of these drugs is most effective in the treatment of K. pneumoniae meningitis has not yet been determined.

ALPERS, Philadelphia.

MENINGITIS DUE TO KLEBSIELLA PNEUMONIAE. P. A. TRICE and T. E. TOWNSEND, J. A. M. A. **149**:1471 (Aug. 16) 1952.

Two cases of meningitis due to Klebsiella pneumoniae are reported. The first patient, a child of 2 years, was moribund on admission and died an hour and 20 minutes after admission. There was no time for treatment except supportive measures, to which the child failed to respond. The diagnosis was made at autopsy.

The second patient, an infant born prematurely, had symptoms of meningitis when 26 days old. The organism obtained from spinal fluid culture resembled K. pneumoniae. Sensitivity studies indicated that the organism was most sensitive to chloramphenicol, which was subsequently administered. The patient's condition was poor. Three days later the fontanel became tense, and two days later generalized clonic convulsions developed. On the 10th day after onset no spinal fluid could be obtained by lumbar puncture. It was thought that the flow of fluid was obstructed by fibrinous exudate.

Definite improvement followed an initial intrathecal injection of 125,000 units of streptokinase and 25,000 units of streptodornase. Prior to the use of these fibrinolytic agents, the anterior fontanel was consistently distended, and there was gradual increase in the circumference of the head. After the first injection of streptokinase and streptodornase, the fontanel remained soft, and the circumference of the head remained the same. However, lumbar puncture was still not productive of spinal fluid.

The patient was discharged after about a month, with a diagnosis of prematurity and meningitis due to K. pneumoniae, with acquired hydrocephalus. Suggested follow-up therapy was not carried out. The child was readmitted at the age of 4 months with pronounced distention of the anterior fontanel and hydrocephalus. Streptokinase and streptodornase were again given by daily intrathecal injections, but with minimal benefit. The patient was removed from the hospital 26 days later and died at home after 2 weeks.

Trice and Townsend feel that some benefit was obtained from the use of streptokinase and streptodornase and suggest further investigation of the use of these agents in cases of meningitis in which block of the circulating cerebrospinal fluid occurs. No untoward results were noted from their use.

ALPERS, Philadelphia.

EXTRADURAL CEREBELLAR HEMATOMA. A. J. BELLER and E. PEYSER, J. Neurosurg. **9**:291 (May) 1952.

The authors present three cases of extradural cerebellar hematoma, in one of which operation was successful whereas in the other two the outcome was fatal. The literature on this subject is reviewed, and the clinical features and main findings are discussed.

Beller and Peyser point out that epidural bleeding into the posterior fossa of the base of the skull should be suspected in cases of trauma to the back of the head when signs of increased intracranial pressure and abnormal neurological findings, either cerebellar or noncerebellar, appear together after a lucid interval, which, however, need not invariably be present. The condition usually develops more slowly than epidural hematoma in the middle fossa, since the bleeding is always venous. External signs of injury, as well as plain roentgenograms, may be helpful in the correct diagnosis and exact localization of the lesion.

Rigidity of the neck and cerebellar signs usually indicate a lesion in the posterior fossa. Pyramidal tract signs, whether homolateral or contralateral, neither exclude nor prove this diagnosis. Occasionally a sign of third nerve involvement occurs, but should not lead to the exclusion of an infratentorial lesion. Although no definite explanation of this phenomenon can be given, that of pressure on the nerve from below is most likely.

The only therapeutic measure which may offer success is surgical removal of the clot and sealing off of the origin of bleeding. The authors advocate infratentorial exploration in any case in which the history and clinical findings arouse suspicion.

ALPERS, Philadelphia.

Diseases of the Brain

SURGICAL CARE OF THE NEUROLOGICALLY DEFECTIVE INFANT. J. MARTIN, A. M. A. Arch. Surg. **65**:150 (July) 1952.

Many physicians assume an attitude of unwarranted defeatism when dealing with a neurologically defective infant.

Martin takes issue with this undue pessimism. First, every child with a neurologic defect should be subjected to a thorough neurologic examination, using all modern technical means to determine the gross anatomic changes and disturbances of function. No matter how hopeless the situation may seem at first glance, precise diagnosis may point the way to successful surgical management. For example, an infant whose signs and symptoms suggest hopeless hydrocephalus may in reality harbor a favorable subdural hematoma, which can be cured by operation. In selected cases, internal hydrocephalus may be either arrested or improved by removal of the causative lesion or by restoration of the cerebrospinal fluid circulation. Surgical treatment of craniostenosis has given encouraging results if undertaken at an early stage. In cases of myelomeningocele operative repair is often worth while, even though there may be permanent neurologic defects.

LIST, Grand Rapids, Mich.

METHODS FOR THE EARLY DIAGNOSIS OF MULTIPLE SCLEROSIS: OBSERVATIONS WITH SPECIAL REFERENCE TO THE SO-CALLED OCULAR TYPE. O. LOWENSTEIN, A. M. A. Arch. Ophth. **46**:513 (Nov.) 1951.

Lowenstein believes that pupillography may reveal information making possible an early diagnosis. Four cases are reported in substantiation of his conclusions. The first case was one of a lesion in the optic nerve. In this case pupillographic studies with light stimulation of the right eye resulted in direct and consensual reactions of 2.6 mm., while stimulation of the left eye resulted in direct and consensual reactions of only 2.0 mm. Throughout the series of reactions, the reflexes elicited from the left eye were less extensive than those elicited from the right eye, indicating that the conductibility of the left optic nerve was diminished; this confirmed a previously established, but later doubted, diagnosis of retrobulbar neuritis.

In the second case, one of a lesion of the fibers connecting the pretectal area and the third nerve nucleus, pupiliary studies showed anisocoria, with a difference of about 0.8 mm., which increased to about 1 mm. at the peak of the contraction, when the right (smaller) pupil was stimulated directly by light of average intensity, and decreased to practically zero when the left (larger) pupil was directly stimulated. The phenomenon was accentuated by prolonged or high-intensity illumination, indicating weakness of the consensual reaction to light in either pupil.

The third case was one of a lesion in the third nerve, the efferent pathway. In this case the pupillographic studies showed that after adaptation to darkness the left pupil (7 mm.) was slightly larger than the right pupil (6.7 mm.). The reaction of the left pupil to light was sluggish and inextensive, amounting to no more than 1 mm., both on direct and on indirect stimulation. The reaction of the left pupil to near vision was also slow and inextensive. Reactions of the right pupil to light and in near vision were prompt and amounted to 3.5 mm. The shape of the reactions of the left pupil showed that the disturbance was parasympathetic, concerned with the third nerve nucleus or the pathways peripheral to it. The fact that psychodilation was normal on both sides indicated that the lesion was central to the ciliary ganglion.

In the fourth case, one of lesions in the hypothalamus and in the fibers connecting the pretectal area and the third nerve nucleus, pupillographic studies revealed the following symptoms: (1) bilateral tonohaptic shape of the light reflexes, indicating a lesion in the posterior part of the hypothalamus or the midbrain cephalad to the third nerve nucleus, and (2) weakness of the consensual reaction to light when either eye was stimulated, pointing to a lesion in the fibers connecting the pretectal area and the third nerve nucleus.

SPAETH, Philadelphia.

SEVERE OPTIC NEURITIS IN INFECTIOUS MONONUCLEOSIS. T. W. BONYNGE and K. O. VON HAGEN, J. A. M. A. **148**:933 (March 15) 1952.

Infectious mononucleosis may involve several systems of the body, and its clinical course is greatly varied and utterly unpredictable. Bonynge and Von Hagen report a case of infectious mononucleosis in a 14-year-old girl in which marked visual impairment was the presenting complaint and moderately severe optic neuritis was the only prominent sign. Recovery was complete.

Dimercaprol injection U. S. P. (BAL) has been used, with apparent success, in treatment of peripheral neuropathies, and the drug was employed in this case with suggestively encouraging results. The patient's sight was slowly improving when dimercaprol therapy was started. However, pronounced, rapid improvement in visual acuity was shown within 24 hours after administration of dimercaprol. This tendency continued during the seven days of dimercaprol therapy, during which time a total dose of 700 mg. was administered. Twelve weeks after onset examination revealed 20/20 vision in each eye, some optic nerve atrophy, normal visual fields, and normal color perception.

Gamma globulin has been reported by Bower to give good results in the treatment of infectious mononucleosis.

Fortunately, in many instances secondary optic neuritis regresses, with no permanent residual visual impairment. However, there is always the possibility that permanent visual impairment will result in certain cases of optic neuritis. With the increasing numbers of cases and the bizarre manifestations occurring in infectious mononucleosis, the authors suggest that in all these cases the possibility of involvement of the peripheral or central nervous system be anticipated, so that treatment with dimercaprol injection and/or gamma globulin may be instituted as early as possible.

ALPERS, Philadelphia.

INCREASED INTRACRANIAL PRESSURE IN EMPHYSEMA CAUSED BY OXYGEN INHALATION. J. C. MITHOEFER, J. A. M. A. **149**:1116 (July 19) 1952.

In some patients with pulmonary emphysema the administration of high concentration of oxygen results in mental changes ranging from somnolence to coma, and sometimes death. Mithoefer studied the effect of oxygen and carbon dioxide inhalations on the pulmonary ventila-

tion and spinal fluid pressure of four patients with chronic pulmonary emphysema and three normal subjects in an effort to elucidate the mechanism of production of this phenomenon.

The author found that the inhalation of carbon dioxide by normal subjects increases the spinal fluid pressure through cerebral vasodilatation. In two of the patients with pulmonary emphysema, oxygen inhalation resulted in respiratory depression, carbon dioxide retention, and increased intracranial pressure. The author discusses the possible mechanisms for the production of this sequence of events and the mental changes produced in the patients. Occasional periods of hyperventilation during oxygen therapy will prevent the development of these undesirable effects.

ALPERS, Philadelphia.

MULTIPLE SPINAL CORD MENINGIOMAS. R. W. RAND, J. Neurosurg. **9**:310 (May) 1952.

The incidence of multiple meningioma is small as compared with the frequency of the single occurrence of this tumor, and in most instances of multiplicity the lesions are intracranial or intracranial and spinal. Rand describes the case of a woman aged 34 from whom meningiomas were removed at the sixth and third thoracic levels. The patient presented no stigmata of neurofibromatosis.

The clinical and x-ray findings in this case clearly indicated a solitary tumor at the level of the fifth thoracic vertebra. The sensory level was very definite at the seventh thoracic dermatome, with no evidence of disturbance superiorly. The multiplicity of the lesions was clinically unsuspected in this case, the second meningioma being the silent partner.

When one is dealing with neoplasms of the spinal cord, the possibility of concealed, asymptomatic multiple tumors must be borne in mind. After the removal of a neoplasm Rand advises further exploration of the spinal canal by passage of a catheter. Myelographic studies should be carried out several weeks after operation if the results of the operation do not come up to expectation.

The patient reported on, after postoperative paraplegia due to edema of the spinal cord, made a complete recovery. The tumors in this instance were typical psammomatous meningiomas.

ALPERS, Philadelphia.

ELECTROENCEPHALOGRAPHIC STUDY OF PATIENTS WITH TUBEROUS SCLEROSIS. W. W. DICKERSON and C. D. HELLMAN, Neurology **2**:248 (May-June) 1952.

Tuberous sclerosis (Bourneville's disease) is characterized by epilepsy, adenoma sebaceum, and mental deficiency. In an electroencephalographic study of 29 patients with this disease, a total of 58 electroencephalograms were completed. All patients but one were institutionalized.

The authors found no specific or common pattern in the recordings in this study. It was noted that the percentage of normal records was less than that in 3,000 recordings of institutionalized epileptic patients. Focal abnormalities were common, but these were not specific. No single feature was found which could distinguish the records of these patients from those of patients who have epilepsy, mental deficiency, or other forms of organic brain disease. It was not possible to localize the tuberous nodules in the brain characteristic of the disease.

The electroencephalograms of blood relatives of patients with tuberous sclerosis were similar to the records published previously by Robinson for relatives of epileptic patients without tuberous sclerosis.

ALPERS, Philadelphia.

ENVIRONMENTAL STUDIES IN MULTIPLE SCLEROSIS. G. STEINER, Neurology **2**:260 (May-June) 1952.

Recent mortality and morbidity statistics show that there is a definite geographic distribution in the occurrence of multiple sclerosis. Steiner undertook this environmental study in the state of Michigan. The 500 cases surveyed came from two sources: One-third were cases in which examinations and clinical evaluations were made in the Multiple Sclerosis Center of Detroit, and two-thirds were cases obtained from questionnaire surveys of medical sources. The results were the same in the two groups.

From his survey, Steiner concludes that there is no man-to-man transfer. There is no transovarian passage. A particular environmental extrahuman reservoir of the disease agent is highly probable. This extrahuman reservoir and its accumulation in the environment of certain

groups, namely, patients sharing the same household or the same special occupation, are responsible for the higher incidence in household groups (families) and among teachers, especially kindergarten and elementary school teachers, particularly in rural areas. In the same household, siblings are more exposed to the extrahuman source than are persons in the paternal-filial combination.

Dogs or cats may be suspected as reservoirs of the agent. Insect vectors as links in the chain of transmission may be significant.

ALPERS, Philadelphia.

NEUROFIBROMA OF THE TRIGEMINAL NERVE ROOT IN THE POSTERIOR FOSSA: TOTAL REMOVAL BY TRANSTENTORIAL APPROACH. G. S. BAKER, and A. A. BAILLEY, Proc. Staff Meet., Mayo Clin. **27**:118 (March 12) 1952.

Baker and Bailley describe the case of a man aged 34 in which the outstanding symptoms and observations made over a period of five years pointed to a lesion affecting primarily the fifth cranial nerve root, with pressure on the pons cerebelli and cerebellum as a secondary manifestation. An operation performed four years previously had been unsuccessful in reaching the tumor by a suboccipital approach. In view of this fact, and with x-ray evidence of erosion of the tip of the petrous portion of the temporal lobe, a transtentorial approach to the lesion was considered the best surgical route. A cystic tumor about the size of a golf ball was found. When the fluid of the mass was removed, the capsule and solid portion of the tumor could be entirely enucleated with relative ease. The patient was discharged from the hospital on the ninth postoperative day, in a greatly improved condition.

From a neurosurgical standpoint the authors feel that the transtentorial approach for tumors of the fifth cranial nerve root which are located high in the cerebellopontine angle is very satisfactory. The same approach for meningiomas arising from both sides of the tentorium can be used. However, tumors of the acoustic nerve are best approached by suboccipital craniotomy.

ALPERS, Philadelphia.

BEHCET'S DISEASE WITH MENINGOENCEPHALITIC INVOLVEMENT. SALLUSTIO MAGNI, Riv. oto-neuro-oftal. **26**:445 (Sept.-Oct) 1951.

A man aged 27 while in military service in Libya began to have recurring attacks of muscle and joint pains, which lasted four or five days and which came on once or twice a month. After a few months he began to complain of recurring inflammation of the eyes. These were attacks of uveitis with hypopyon. While he was under observation, there appeared lesions on his tongue and lower lip, with later ulceration. After five years of attacks of uveitis, hypopyon, and buccal lesions, he one day had transitory weakness of the left lower limb. A few months later he had sudden onset of a very severe headache, a tendency to profanity, dysarthria, and fever. On his admission to the hospital, the following significant neurologic signs were noted: ataxia of the lower limbs; limitation of elevation of the right eye, weakness of the right side of the face, nonmimetic in type, dysdiadokokinesis, hyperreflexia in the left upper and the right lower extremities, and bilateral extensor responses to plantar stimulation. The pupillary reactions were unreliable because of synechiae. A lumbar puncture one month after the appearance of these neurologic manifestations showed 9 cells per cubic millimeter and a total protein content of 160 mg. per 100 cc.

During the next two years he had a few exacerbations of ocular inflammation with no change in the neurologic picture. Then one day he suddenly became ataxic and could not stand. The exacerbation of neurologic manifestations was accompanied by recurring uveitis and hypopyon. Examination this time revealed amimia, mild bilateral ptosis, more marked on the right than on the left, nystagmoid jerks on looking to the right, fixed and irregular pupils, a mild facial weakness, bilateral Babinski signs, tremor of the jaw and upper limbs, and confusion and puerilism. The spinal fluid contained 18 cells per cubic millimeter, with marked increase of protein. There was a febrile rise during the exacerbation. The patient died of cardiovascular failure.

Autopsy showed passive congestion of the viscera, mild arteriosclerosis, degenerative changes in the myocardium, and thickening of the leptomeninges. There were cellular infiltration of the

meninges and degenerative ganglion cell changes, especially in the basal nuclei, accompanied by mild glial proliferation. There was a considerable amount of perivascular infiltration with polymorphonuclear cells, with some hemorrhage, in the region of the mesencephalon. No inflammatory infiltration was noted in the cornea and sclera of either eye. The irides showed diffuse atrophy of connective tissue with some cellular infiltration; atrophy of the choroid was marked in the superior half of the right eye and less pronounced in other regions. There was definite cellular infiltration of the retinae and the optic nerves.

The author believes that there is a definite relation of the ocular and buccal lesions to the involvement of the central nervous sytsem. He emphasizes the simultaneous flaring up of the ocular affection and the increase in the neurologic manifestations. He believes that the lesions were most likely due to a virus infection. Material from the lesions of the buccal cavity and the anterior chamber of the eye during an episode of hypopyon was studied for herpetic virus, with negative results.

N. Savitsky, New York.

Peripheral and Cranial Nerves

Herpes Zoster Ophthalmicus and Post-Herpetic Neuralgia. W. F. T. Tatlow, J. Neurol., Neurosurg. & Psychiat. **15**:45 (Feb.) 1952.

Fifty-eight unselected patients who had had herpes zoster ophthalmicus were studied with special reference to the incidence of postherpetic pain.

The average age at time of onset was 53.7 years. There was no significant difference in the sex incidence. Of the 58 patients, none showed involvement of any division other than the first, corroborating the findings of other authors that involvement of other divisions is rare.

Forty-seven of the patients were traced, and only 1 had been given alcohol injection for severe pain. Twenty-nine patients were examined, and of these 7 had persistent pain or abnormal sensation. The seven patients with pain or abnormal sensations were all found to have diminution of some sensory modalities. Five other patients examined also had sensory diminution but did not have pain or other abnormal sensation.

Six of the 29 patients examined had pupils which did not react at all to light either directly or consensually, but reacted well in accommodation. Tatlow suggests that the site of the lesion accountable for these pseudo Argyll Robertson pupils may be in the ciliary ganglion.

Alpers, Philadelphia.

Section of Optic Nerve in the Optic Canal: Late Removal of Bony Fragment. D. Sabbadini, Riv. oto-neuro-oftal. **26**:399 (Oct.) 1951.

Sabbadini reports a case of a man aged 31 who sustained a very severe head injury, with otorrhagia and loss of consciousness. Six days after the accident there were ecchymoses around both eyes. The left eye was closed by edema, with mucopurulent secretion and escaping vitreous from a laceration near the upper end of the cornea. The anterior chamber of the left eye was cloudy. One right side, there were edema, ptosis, chemosis, and bleeding in the inferior part of the eyeball, the pupil could be widened by atropine, and the fundus showed evidence of commotio retinae around the disk and in the foveal area. There was absence of light perception on the right, some meningeal signs, and mild clouding of the sensorium. A roentgenogram showed definite deformation of the right optic canal, which appeared oblong, the longer diameter being the vertical. In the center of the canal was a triangular shadow, with base medial and apex lateral. The apex of this triangular shadow seemed to be in contact with the lateral wall of the right optic canal. The x-ray findings pointed to a fragment of bone from the optic canal apparently cutting into the optic nerve. An intracranial operation revealed two bony fragments in the right optic canal; the larger one was in the optic canal, as noted on x-ray examination. The optic nerve was almost completely cut across by this bony fragment. While part of the bony fragment was being removed, the patient reported some light sensation, due apparently to the surgeon's having touched the distal portion of the nerve with his instrument. There was no improvement of vision following removal of the fragments. Operation was done with the hope that perhaps some optic nerve tissue was spared. It was not done earlier because of the presence of meningeal infection.

N. Savitsky, New York.

THE SEVENTH CRANIAL NERVE IN ACOUSTIC NEUROMA. C. AMBROSETTO, Riv. oto-neuro-oftal. **26**:549 (Nov.-Dec.) 1951.

Severe involvement of the seventh cranial nerve is exceptional in cases of acoustic neuroma. Mild and partial damage is encountered more frequently. Ambrosetto reports his observations on the impairment of the seventh nerve in 17 verified cases of acoustic neuroma. In two cases with relatively large tumors there was no evidence of involvement of the seventh nerve. In one case with a long history and a large tumor, with increased intracranial pressure, involvement of the seventh nerve was limited to mild weakness of the orbicularis muscle of a few months' duration. In seven cases there was moderate evidence of impairment of seventh-nerve function. In four of these seven cases all three divisions were involved; in two cases only the third, and in one case only the first. In two instances with mild weakness of the facial nerve there were clonic twitches of the face, limited to the chin in one and involving the whole face in the other. In one case there was a mild increase of tone in the facial muscles on the side of the tumor; this increase was evident at rest and was associated with weakness in the third division. In two cases only mimetic facial weakness was noted on the side of the neoplasm. In one case there was a marked paresis of all three divisions of the seventh nerve, with involvement of the other cranial nerves of the posterior fossa on the same side. Taste was investigated in nine cases; it was impaired in the anterior two-thirds of the tongue in four and on the whole of the side of the tongue ipsilateral to the tumor in one. There was no clear relation between degree of involvement of the fifth and that of the seventh cranial nerve. The relative sparing of the seventh nerve is due to the fact that in the region of the angle it can be readily displaced by slowly growing tumor tissue because of its looseness and mobility.

N. SAVITSKY, New York.

News and Comment

JOINT MEETING OF GERMAN SOCIETIES

The German Society of Neurology, the German Society of Neurosurgery, and the German Society of Neurologists and Psychiatrists will hold a combined meeting in Munich Aug. 26 to 29, 1953. On the first day the subject will be Technique of Narcosis; on the second, Meningitis, and on the third, Development of Psychiatry in the United States During the Last Three Decades. Psychodiagnostics will be the subject for the last day. The German Neuropathological Society will hold its meeting in Munich concurrently, Aug. 26 to 27. The subject will be The Cerebellum. For information, write Dr. Ehrhardt, Universitäts-Nervenklinik, Marburg/Iahn, Germany.

THE EIGHTEENTH INTERNATIONAL CONGRESS OF OTONEURO-OPHTHALMOLOGY

The Eighteenth International Congress of Otoneuro-Ophthalmology will be held in Bologna, Italy, May 3 to 7, 1953; chairman, Prof. Q. di Marzio. The official program follows.

I. Dysraphia in Otoneuro-Ophthalmology
Embryology, Krabbe, Copenhagen
Neurology, Vercelli, Milan
Radioneurology, Mascherpa, Milan
Otolaryngology, Arslan, Padua
Ophthalmology, Franceschetti, Geneva
Neurosurgery, Fasiani, Milan
Facial Surgery, Sanvenero-Rosselli, Milan
General reporter: Belloni, Padua

II. Ménière's Disease
Neurology, Barré, Strasbourg
Otology, Greiner, Strasbourg
Neurosurgery, Tolosa, Barcelona

The official languages are Italian, English, German, French, and Spanish.

Besides the papers on subjects indicated above, papers will be accepted discussing at least two of the specialities at the same time.

Colleagues interested in attending the Congress are requested to give their names and addresses immediately, so that they may be sent a provisional program, in which they will find all explanations about registration, facilities at their disposal, and railroad transportation.

Anyone who wishes to submit a paper or to take part in the discussions should apply to the general secretary, Dr. Giuseppe Cristini, Clinica Oculistica-Policlinico, Bologna, Italy.

AMERICAN PSYCHOSOMATIC SOCIETY

The American Psychosomatic Society has changed the dates of its coming annual meeting. Instead of taking place in May, the meeting will be held on April 18 and 19, 1953, at Chalfonte-Haddon Hall, in Atlantic City.

THE NATIONAL PARAPLEGIA FOUNDATION

The National Paraplegia Foundation wishes to announce the continuation of a limited number of fellowships for research in spinal cord disease and trauma and in the complications commonly associated with such disease or injury. These fellowships carry a minimum stipend of $3,000 per year and may be awarded to any candidate who has demonstrated a capacity for medical research and has outlined a program of meritorious study. The fellowships will be awarded by the Medical Advisory Committee and are open for award for the academic year 1953-1954. Application forms may be obtained from the chairman of the Medical Advisory Committee, L. W. Freeman, M.D., and applications should be submitted to him not later than May 1, 1953.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

At the thirty-second annual meeting of the Association for Research in Nervous and Mental Disease held in New York on Dec. 12 to 13, 1952, the following officers were elected for 1953:

President, Dr. Davenport Hooker; first vice-president, Dr. John C. Whitehorn; second vice-president, Dr. Lawrence H. Snyder; secretary-treasurer, Dr. Clarence C. Hare; assistant secretary, Dr. Rollo J. Masselink.

The subject for the 1953 meeting will be "Genetics and the Inheritance of Integrated Neurological and Psychiatric Patterns."

DR. ROBERT A. COHEN APPOINTED CLINICAL DIRECTOR OF NATIONAL INSTITUTE OF MENTAL HEALTH

Dr. Robert A. Cohen has been appointed Clinical Director of the National Institute of Mental Health, it was announced today by Dr. Leonard A. Scheele, Surgeon General of the Public Health Service, Federal Security Agency. Dr. Cohen comes to the Public Health Service from Chestnut Lodge Sanitarium, Rockville, Md., where he has been Clinical Director since 1948.

As head of clinical investigations for the Institute of Mental Health Dr. Cohen will be responsible for conducting a program of clinical research in mental diseases and psychotherapy in the Clinical Center nearing completion at the National Institutes of Health at Bethesda. In addition to his experience in psychiatry, Dr. Cohen brings to his new post an extensive background in the anatomy, physiology, and biochemistry of the nervous system.

Dr. Cohen received both his degree of Doctor of Medicine and his degree of Doctor of Philosophy in neurophysiology from the University of Chicago in 1935. He entered psychiatric training at Johns Hopkins University under Dr. Adolf Meyer in 1937. After completion of his residency training at Sheppard and Enoch Pratt Hospital, in Towson, Md., and the Institute for Juvenile Research in Chicago, Dr. Cohen served successively on the staffs of Sheppard and Enoch Pratt Hospital, the Washington (D. C.) School of Psychiatry, and Chestnut Lodge Sanitarium.

From 1941 to 1946 Dr. Cohen served as a medical officer in the United States Navy. He is a member of the Panel on Human Relations of the Research and Development Board, Department of Defense, and since 1946 has been a consultant in psychiatry at the National Naval Medical Center, Bethesda. He is a fellow of the American Psychiatric Association; diplomate of the American Board of Psychiatry and Neurology; fellow of the Washington (D. C.) School of Psychiatry; councillor of the Washington Psychiatric Society; president of the Washington Psychoanalytic Society; member of the American Psychoanalytic Association and chairman of its committee on naval fellowships, Board of Professional Standards, and secretary of the education committee of the Washington Psychoanalytic Institute.

THE AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology is again offering special courses in various aspects of neurology and allied disciplines. The popularity of the courses given in previous years has resulted in nine courses being offered this year. Courses in neuropathology and clinical electroencephalography are being repeated, as is the course in neuroroentgenology. The latter course has proved so popular that it will be presented as a two-day course this year, with a wealth of material. Other courses to be presented this year are Special Problems in Clinical Electroencephalography, Episodic Disturbances of the Nervous System, Clinical Neuro-Ophthalmology, Language Disabilities, Brain Tumors, and Neurological Anatomy.

These courses are oriented toward practical clinical use for the one who is establishing a basic foundation and for the one looking for advanced knowledge. The faculty has been selected, many from the allied specialties, for recognized leadership in their field and for their teaching ability.

Fees are moderate, and many courses offer atlases, loan boxes of slides, syllabuses, discussion sessions, etc. Modern projection techniques will be used to demonstrate material. Courses will be one-day courses except, as mentioned above, the two-day course in neuroroentgenology. There will be three days (April 6, 7, and 8) of special courses preceding the fifth annual meeting of the Academy. Courses and meeting will be held at the Edgewater Beach Hotel, Chicago. Details can be obtained by writing Mrs. J. C. McKinley, 19 Millard Hall, University of Minnesota, Minneapolis.

Books

Treatment of Mental Disorder. By Leo Alexander, M.D. Price not given. Pp. 507, with 143 figures and 22 tables. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia, 5, 1953.

"A poet once remarked that the gifts of life are thus distributed that, alas, we are given either the wine or the cup, seldom both together. I think he was referring to the wine of the vitality of youth and to the cup of wisdom and experience. I should like to paraphrase this simile, alluding to the increased zest resulting from relief of anxiety and depression, the basic physical change of mood readily afforded by physical treatments, as the wine; and to the understanding of psychodynamics and the appreciation of emotional needs resulting therefrom as the cup. Alas, the wine of physical treatment is too often spilled without the cup. But the cup alone, beautifully designed and crystal clear though it may be, will be void of substance—the zest of vitality that is often the primary need of the sick person.

"In this book, I ventured to outline how the wine and the cup can be brought together. It is difficult for me to understand why so many adherents of physical treatment should have failed to avail themselves of the cup of psychodynamic understanding, and why so many in the field of psychodynamics should disdainfully reject the wine of physical treatment with a vehemence comparable to that of the crusading ascetic."

The author thus outlines his varied approach to the problem of mental disorder, stressing both the physical and the psychodynamic, and blending the two. He builds up defenses in some instances, and demolishes them in others, preparatory to building better ones. He looks not at the diagnosis, but at the stage of the illness and the mechanisms that are susceptible of modification, first by one means, then by another.

Theories come and go, but sick persons remain, and physicians to treat them. Illuminating examples are given of the way in which sick people are returned to health by application of various treatments. Alexander stresses particularly such symptoms as anxiety and depression. Depression is strikingly relieved by electroconvulsive shock, while anxiety is enhanced. Nonconvulsive stimulation reduces anxiety, but exaggerates depression; therefore, a combination or alternation of the two may be required. Or if the combination fails, insulin shock is preferable, or lobotomy. Theoretical considerations are presented in detail, but the practical applications are also given due weight. In order that the patient may enter into the therapeutic session with meaningful experiences, he must be relieved of the overwhelming emotional distress. However, merely to apply physical treatments leaves the patient wide open to renewal of trouble under stressful circumstances unless the period of health is employed to strengthen the patient and to aid him in attaining insight. Psychotherapy is given considerable space, indications for hypnosis, abreaction, suggestion, persuasion, and simple reassurance being allotted their due emphasis. The author states, however: "This trend [reliance upon psychotherapy alone] goes on in spite of the fact that even now no scientific proof has been established that the major mental illnesses are at all significantly modifiable by purely psychologic means. This is an example of how major trends of scientific endeavor go on for a time unchecked by the impact of reality."

Alexander brings together large statistics from various published works—2,577 schizophrenic patients treated by intensive psychotherapy as compared with 12,716 control patients given custodial and supportive care alone. "We are forced to conclude from this finding that the addition of intensive psychotherapy to the therapeutic regimen in schizophrenia does not increase the number of patients who are going to improve, but helps a significant portion of those who are improving to achieve a better quality of improvement." Analysis of 14,081 patients treated by convulsive shock therapy shows therapeutic results considerably higher than those obtained under custodial care. Such convulsive shock treatment is the method of choice in depressions, although it is somewhat effective in other conditions. Anxiety is an indication for treatment with nonconvulsive electric treatment, electric coma, or insulin subshock,

sometimes followed and reinforced by insulin shock. The use of the nonconvulsive methods and the rapid arousal from insulin coma furnish the physician with a patient who is more receptive to psychotherapy.

Considerable reliance is placed by Alexander upon the Funkenstein test for autonomic imbalance. A high level of anxiety precipitable by intravenous injection of epinephrine, 0.25 mg., contraindicates convulsive shock therapy, whereas a marked fall in blood pressure on administration of 10 mg. of methacholine (mecholyl®) presages an increase in depression following nonconvulsive treatment. The methods of administering both the convulsive and the nonconvulsive treatments are given in detail, probably more so than will be found practical, since each therapist will employ his own modifications. The eleven steps described seem to shade into one another. Practical hints are given for the prevention of the clonic stage in convulsive shock, as well as for the prevention of the complications of these methods.

Insulin shock is preferred in the treatment of severe mental disorders, particularly of the schizophrenic variety. Here an analysis of 9,483 published cases as compared with 11,080 controls showed that clinical improvement occurred in 61% instead of 29%. Patients with a manic-depressive psychosis in the manic phase show an even greater rate, 91%, with results almost as good in certain involutional depressions.

"It is my considered opinion that lobotomy in cases of mental illness is only indicated when adequate amounts of other forms of physical treatment have failed." Alexander's reasons are that some risk of psychic loss is practically inevitable, that undesirable side-effects may persist, and that "the intensity of the illness as tested by treatment resistance also permits the team of neurosurgeon and neuropsychiatrist adequately to gauge the extent of the operation to be performed." Lobotomy is preferred to repeated courses of shock therapy when relapses are rapid and severe, and in older patients with obsessive trends who are disturbed by memory losses following shock methods. Lobotomy is by no means the final word. Frequently this procedure is followed not only by psychotherapy, chiefly of the directive and supportive type, but also by electric shock or insulin shock treatment, which may be more effective after operation than before. As a result of all these approaches, according to the author, none of his schizophrenic patients in the past five years has had to return to the hospital.

"In actual practice, therefore, there need remain few if any 'hopeless schizophrenics,' provided one is prepared to use the full gamut and range of physical and psychologic treatment methods available."

This is one of the few books on treatment in psychiatry that can be read and studied with profit by the mature psychiatrist, as well as by the beginner. Its print is small, but a wealth of wisdom and ingenuity is packed between its covers.

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